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THE LITERARY AND HISTORICAL ASPECTS OF THE WRITINGS OF SIR WILLIAM OSLER.[1]

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THERE is no better illustration of Sir William Osler's literary ability combined with his historical perspective than the opening paragraph of "Michael Servetus" (Osler, 1909):

> The year 1553 saw Europe full of tragedies, and to the earnest student of the Bible it must have seemed as if the days had come for the opening of the second seal spoken of in the Book of Revelation, when peace should be taken from the earth and men should kill one another. One of these tragedies has a mournful interest this year (1909), the four hundredth anniversary of the birth of its chief actor; yet it was but one of thousands of similar cases with which the history of the sixteenth century is stained. On October 27, shortly after twelve o'clock, a procession started from the town-hall of Geneva—the chief magistrates of the city, the clergy in their robes, the Lieutenant Criminel and other officers on horseback, a guard of mounted archers, the citizens, with a motley crowd of followers, and in their midst, with arms bound, in shabby dirty clothes, walked a man of middle age, whose intellectual face bore the marks of long suffering. [Osler then describes the walk up the hill outside the city, the fateful stake, the heaped-up bundle of faggots, the large stack of manuscripts and a thick printed book tied round the victim's waist, and the piercing cry he gave as the flames flashed in his eyes.] Thus died, in his forty-fourth year, Michael Servetus Villanovanus, physician, physiologist, and heretic. Strange, is it not, that could he have cried, "Jesu, thou Eternal Son of God" even at this last moment, the chains would have been unwound, the chaplet removed, and the faggots scattered; but he remained faithful unto death to what he believed was the *Truth* as revealed in the Bible.

To paint a picture as vivid, as dramatic, and yet as restrained as this necessitates a complete appreciation of the temper of the mind of the times. This Osler had as a result of extensive readings in early sixteenth century books and manuscripts. In order to make his subjects live again after the *rigor mortis* of immortality had set in, or to bring to life a wholly forgotten man such as his "Alabama Student", Sir William turned the light of his vast knowledge on them to come away with a view neither medical nor poetic but fully rounded. His biographical essays, of course, show him at his best in combining historical and literary talents; yet they are but one part of his extensive writings.

For the purposes of this paper, one might classify these writings as follows: (i) biographical essays, (ii) inspirational essays or lay sermons, (iii) pedagogical essays, and (iv) literary investigations. Although the bulk of his "inkpot career", as he called it, is largely concerned with medical writings of a technical nature—his bibliography lists some 800 titles—with these I am not primarily concerned. This does not at all mean that they do not possess high literary and historical merit. There is, for example, the oft-cited remark of a former Bodley librarian, Falconer Madan, who said that Osler, in his text-book "The Principles and Practice of Medicine", "succeeded in making a scientific treatise literature". A chapter from this book was actually used in an anthology of selections from recent American and English literature called "This Generation" (Anderson and Walton, 1939). On reading the text-book, his papers, his many essays, no one can avoid coming to the conclusion that the innumerable classical and historical allusions and the wealth of literary

[1] Read at a meeting of the Section of Medical Literature and History, Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

flavour must have been born of tremendously wide reading and research. The late Dr. Harvey Cushing's "Life of Sir William Osler" and the keen critical annotations of the enormous "*Bibliotheca Osleriana*" give sufficient proof of this. One could surely get a liberal education in history and literature merely by tracking down all his quotations and allusions. One essay alone, "Science and Immortality", contains quotations from the Bible (the Books of Job, Esdras, Psalms, Galatians, Isaiah, Ecclesiastes, Acts, Corinthians, and Matthew), Aristotle, Plato, Homer, Horace, Terence, Goethe, Sir Thomas Browne, Richard Burton, Donne, Shakespeare, Milton, Montaigne, Shelley, Tennyson, Pater, Stephen Phillips, the "Rubaiyat", Oliver Wendell Holmes, and Jowett on "Buddhism". This does not include allusions to various topics without quoting.

Sir William Osler was never all doctor: it could never have fallen to a genius of his stature to be all any one thing. His eminence as a physician and a professor of medicine has tended to obscure his greatness as an author and his contributions to medical history. Almost thirty years ago the well-known American critic, Christopher Morley, said that Osler's "honorable place as a man of letters" ought to be "more generally understood" (Morley, 1921). Now, if one adds to Cardinal Newman's definition that "literature expresses, not objective truth, as it is called, but subjective; not things, but thoughts", Matthew Arnold's dictum that literature is a "criticism of life", it may easily be seen that literature is an argument concerning ideas. This is distinct from science as an argument concerning things. Therefore, to use this specific connotation, Osler was, in the widest sense of the word, a man of letters. On the other hand, the great impetus he gave to the study of medical history in all its aspects is shown by Dr. Raymond Crawfurd's testimony (quoted by Cushing, 1925):

> I saw a great deal of Osler in connection with the Section of History of Medicine at the Royal Society of Medicine. He was its father, and I doubt if it would ever have come into existence but for his quickening influence; . . . his own contributions were few and mainly biographical, and I do not think anyone could have discovered from them how fully he possesses the true historical sense, but his faculty for extracting contributions on every conceivable aspect of medicine from the most unproductive sources was invaluable to the Section.

Osler's stimulus is seen in his Silliman lectures on "The Evolution of Modern Medicine", which he described as "an aeroplane flight over the progress of medicine through the ages". And there is also the comment of J. A. Chatard, of Johns Hopkins University, on Osler's efforts in historical study (Chatard, 1920): "It is only by thus fostering and helping along a search for old truths that the newer ones assume a more crystalline appearance and we are better able to value them in the light of advancing thought."

Biographical Essays.

The biographical essays, then, were written in the spirit of turning up material for medical historians, as well as furnishing a more fully rounded picture than is ordinarily found of the men treated. The sources are vast, both of primary and secondary material; he collected every edition of Sir Thomas Browne's "*Religio medici*"; his 7000-volume "*Bibliotheca Osleriana*" contains more than 250 by and about William Harvey and more than 200 by and about Browne; and he secured letters, contemporary opinions of his man, periodical articles, and even scraps of out-of-the-way information. "An Alabama Student" grew out of his reading one day an obscure periodical, *Fenner's Southern Medical Reports*, Volume I and II, for 1849-1850 and 1850-1851; but a packet of letters by this unknown Southern doctor, sent to Osler by the physician's daughter, served as the basis for the essay that gives the title to his book, "An Alabama Student and Other Biographical Essays", published by the Oxford University Press in 1908 (Osler, 1908*a*). In telling the story of Dr. John Y. Bassett, of Huntsville, Alabama, Osler rescues from oblivion "one who heard the call and forsook all and followed his ideal"—an account so appreciative it is impossible to read it without feeling a real sympathy for those voiceless,

> for those who never sing,
> But die with all their music in them.

It is not merely the tale of a small-town doctor who leaves his wife and children to study abroad, returns to practise at home, and dies of tuberculosis at forty-six years of age. No glorifier of mediocrity, Osler has made his Alabama student live again because he illustrates perfectly the ideal actions of the average practitioner: leading a commonplace life in a noble way, Dr. Bassett rendered the highest service to his fellow men consistent with his position in life. In humanizing and bringing to life again the frontier physician of mid-nineteenth century America—trials, ideals, almost hopeless aspirations against odds—Osler has presented material necessary before an accurate and appreciative history of the period can be written.

In his essay on Oliver Wendell Holmes (Osler, 1908*a*), written in 1894 shortly after Holmes's death, Osler did not attempt (as he did in "An Alabama Student") to re-create a whole man lest he be entirely forgotten. This time he re-created a whole man lest a significant and important part of him be forgotten. It is Dr. Holmes the author of "The Contagiousness of Puerperal Fever", read in 1843 to the Boston Society for Medical Improvement, and "Puerperal Fever as a Private Pestilence"—this is the side Osler wishes us not to forget. Thus while Holmes's fight against stupidity and bigotry is a landmark in American medical history, these same essays are part of his literary prose and poetry. And Osler quotes this classic paragraph:

> They (students of medicine) naturally have faith in their instructors, turning to them for truth, and taking what they may choose to give them; babies in knowledge, not yet able to tell the breast from the bottle, pumping away for the milk of truth at all that offers, were it nothing better than a professor's shrivelled forefinger.

The Thomas Linacre address (Osler, 1908*b*), as strongly bibliographical as biographical, is a high-point in Osler's essays in the field of medical history. It treats of the life of the great mediæval scholar, of his work as a medical humanist and as a grammarian, and of the Linacre foundations. Of Linacre's place in the English Renaissance, Osler says:

> Not until Greece rose from the dead did light and liberty come to the human mind, and it is the special glory of Linacre that he became, as Fuller says, the "restorer of learning in this country".

And of Linacre as a grammarian:

> Distinguished physicians have often sought and found in fields far remote from the guild, and in literature, and more particularly in science, many have become famous, not a few while still active in practice. . . . So far as we know, Linacre never gave up the pursuit of medicine as a calling, but all through his life the infection of his early studies remained, and in hours of leisure he prepared two works which carried his fame as a grammarian into regions to which the name of the English physician had never penetrated.

The analysis of Linacre's works shows Sir William's mastery of philological criticism; and his carefully balanced treatment of Linacre as "an example of a life of devotion to learning, to medicine and to the interests of humanity" illustrates the highly critical basis upon which Osler worked as a historian.

Once more, in giving a full account of "*Syphilis sive morbus gallicus*" (Verona, 1530) as part of his paper on Fracastorius (Osler, 1908*a*), Osler displays his careful critical taste for historical material. As he had done in the Servetus essay, he sets the scene at the beginning of his story of one of the very few points of light in the history of medicine in the early Renaissance:

> Upon few pictures in literature do we dwell with greater pleasure than that of Catullus returning to his home near Verona, weary with the pleasures of the Capital, sick at heart after the death of his much beloved brother, and still, we may fancy, aching with

> the pangs of misprized love; but at the sight of "Paeninsularum Sirmio insularumque ocellus", he breaks out into joyful song, and all his cares vanish.
>
> Fifteen centuries later another "Bard of Sirmio" sang the joys of the Lago di Garda, "mid Caphian hills", and while we cannot claim for Fracastor a place beside his immortal townsman, he occupies a distinguished position in our annals as the author of the most successful medical poem ever written, and as the man from whom we date our first accurate knowledge of the processes of infection and contagion.

Thus to Osler, Fracastor the poet, sunk now into complete oblivion but for the fact that his poem on syphilis gave the disease its name, is buoyed up by Fracastor the scientific observer in "*De contagionibus*" of typhus, phthisis, and problems of contagion and infection.

In Sir Thomas Browne, Osler was studying and writing about a great man, an inspiration, rather than one who made contributions to the technical advance of medicine. So in his essay on Browne (Osler, 1908*a*) he is more interested in his human side—a seventeenth century doctor who wrote his own creed and who strove to follow a scientific and sensibly sceptical path through life. He ranks him far below Harvey as a scientific man, and apologizes for his belief in witches—"a man must be judged by his times and his surroundings"—in view of the valuable efforts he made to dispel popular superstitions by the scientific methods reported in "*Pseudodoxia epidemica*". In this essay Osler is handing to students of the next generation a sense of the inspiration he himself has got from "*Religio medici*".

Osler departs from this method of treatment in writing of John Locke (Osler, 1908*a*) to tell of a man whose philosophical works are widely read, but whose medical studies and work have been largely forgotten. After fitting newly found data on Locke as a physician into its proportionate place, Osler reminds us that Locke's main business was philosophizing, but that Locke was a physician, and that the pursuit of this profession had a great influence on him. "We may claim Dr. Locke", writes Osler, "as a bright ornament of our profession, not so much for what he did in it, as for the methods which he inculcated and the influence which he exercised upon the English Hippocrates. He has a higher claim as a really great benefactor of humanity, one of the few who 'reflected the human spirit always on the nobler side'."

In these and other biographical studies Osler's well-oriented and historically evaluated observations place us in his debt. As John Ferguson says in "*Bibliotheca chemica*": "What then do these men not owe to him who gathers up their works, and in so doing recalls their achievements, and thus labours to lift that icy pall of oblivion which descends on everything human . . ."

Inspirational Essays.

One gets a charming picture of Sir William from Lady Osler (Cushing, 1925):

> Willie standing in that black-oak pulpit and, in his scarlet gown and velvet cap, looking medieval and wonderful.

This was the Osler so many students, medical and otherwise, came to know at McGill University in Montreal, Canada, at the University of Pennsylvania, at Johns Hopkins University in Baltimore, at the University of Oxford, and at many colleges where he delivered lay sermons. This is the Osler known to so many medical graduates, for even today a public-spirited manufacturing chemist distributes—as he has for several years—a copy of "Aequanimitas", Osler's best known collection of addresses, to every newly-gowned M.D. each commencement day in the United States. "A Way of Life" is presented to Canadian graduates. Probably his most successful work from a literary standpoint, these essays cover the whole field of ethics and manners and aim to inspire young men to do better work in medicine or any other field. Most particularly these essays undertake to make observations upon life, apart from any vocational interest, upon ways in which to extract the last drop of worth from our lives. They contain, says Dr. Cushing, "a deep mine of golden counsel equally suited for others . . . a sense of humour and a love of good literature". As one reviewer has commented (Cushing, 1925):

> It would be well for society in general if all the sermons preached from all the pulpits in Christendom showed the lofty feeling for all that is good and true, the genial wisdom and energizing quality of these discourses.

The considered and organized counsels of one of the best loved physicians of modern times, these addresses draw upon all literature from the classics down to the works of Osler's own time. But the framework into which the web of literary allusion is woven is the product of the author's own fertile mind, stimulated by enormous powers of perception and concentration. The best examples of this type are "Aequanimitas", which gives its title to the volume, "The Student Life", "Man's Redemption of Man", "Science and Immortality" and "A Way of Life".

"Aequanimitas", a word which became his motto on the coat of arms he received on becoming a baronet, is the answer Osler would use if asked: "What one quality must a doctor have to be a success?" This element of imperturbability, misunderstood by the laity and without which physicians betray indecision and worry, and lose their patient's confidence, is acquired by education, practice and experience. "Keen sensibility", wrote Osler (1930), "[must] not interfere with steadiness of hand or coolness of nerve, [but] the human heart by which we live should not be hardened." Osler's mental equivalent to this bodily virtue was summed up by Antoninus Pius on his deathbed in the watchword "Aequanimitas" (Osler, 1930):

> As for him, about to pass *flammantia moenia mundi* (the flaming ramparts of the world), so for you, fresh from Clotho's spindle, a calm equanimity is the desirable attitude. How difficult to attain, yet how necessary in success as in failure.

The original title of "The Student Life" (Osler, 1931), his most popular essay, is "The Student Aged 17 to 70", and this, with the quotation from the Sermon on the Mount prefixed to the published address ("Take therefore no thought for the morrow: for the morrow shall take thought for the things of itself"), explains its theme: education is a lifelong course. Recognized by his desire to know the truth, a steadfastness in its pursuit, and an open, honest heart, free from suspicion, guile and jealousy, the student must be associated with large views—concentration and specialism should not be too narrow. (This idea he reiterated over and over in many essays.)

> The value of a really great student to the country is equal to half a dozen grain elevators or a new transcontinental railway.

If these two essays are literature in that they lift up the mind of man that he may not weary of things material about him and so give up the eternal struggle, then "Man's Redemption of Man" (Osler, 1931) adds to this quality an historical touch. He begins this essay:

> To man there has been published a triple gospel—of his soul, of his goods, of his body. Growing with his growth, preached and professed in a hundred different ways in various ages of the world, these gospels represent the unceasing purpose of his widening thoughts.

The first gospel, he said, brought hope more often than despair; the second—of man's goods—is "written in blood on every page of history"; the third, bringing man into relation with nature—"a true *evangelion*, the glad tidings of conquest beside which all others sink into insignificance—is the final conquest of nature, out of which has come man's redemption of man". Speaking of the curse of disease and pain suffered by man—a picture brightened by the triumph of Greek thought, only to be darkened again by mediævalism—Osler traced the rise of the experimental method which transformed the modern world. He called the introduction of anæsthesia, Lister's great gift of aseptic surgery, and the abolition of fevers and acute infections the three great steps of the growth of modern sanitary science. The then new process of vaccination and the work of those at the Panama Canal indicated further progress to Osler in man's redemption of man. But today,

in 1950, they show us how much more has since been done; yet the gospel of man's goods continues to be written in blood.

"A Way of Life" (Osler, 1926) once more suggests that we should not worry about tomorrow:

> Change that hard saying "Sufficient unto the day is the evil thereof" into "the goodness thereof", since the chief worries of life arise from the foolish habit of looking before and after.

And in giving the Yale students who heard him a philosophy of life, he quoted Walt Whitman watching a group of passing workmen:

> Ah, the glory of the day's work, whether with hand or brain! I have tried
> To exalt the present and the real,
> To teach the average man the glory of his daily work or trade.

A few remarks need be made about Sir William's most suggestive essay, "Science and Immortality" (Osler, 1904). Admitting his presumption in speaking of immortality after so much had been already said, he quoted his beloved Sir Thomas Browne:

> A dialogue between two infants in the womb concerning the state of this world might handsomely illustrate our ignorance of the next, whereof methinks, we yet discourse in Plato's denne—the cave of transitive shadows—and are but embryon philosophers.

The old triple classification of mankind serves as a framework for the paper: the Laodiceans, who believe in immortality, but whose lives are uninfluenced by it; the Gallionans, who put the supernatural altogether out of their lives; and the Teresians, whose faith in eternal life is the controlling influence in this one. The second viewpoint is more common to naturalists and scientists than to those devoted to literature and the humanities, for science has knocked over the notion that a providence "cares for the sparrow and numbers the very hairs on our head". This essay inquires into the depth of man's soul and seeks his higher destiny. Not an argument in favour of immortality—for Osler's attitude betrays doubt—it is a plea for his own *confessio fidei* that he had rather come to the opinion of Cicero, and "be mistaken with Plato than be in the right with those who deny altogether the life after death".

A unifying note runs through all of these inspirational essays: a strong equanimity, based upon a strict stoic philosophy. It is the doctrine of Marcus Aurelius and Epictetus, which Osler finds also in the New Testament dictum to take no thought of tomorrow. Throughout, Osler follows this to its logical application. Incident to the common theme, which is pure literature in both form and substance, other things also receive their expression —advice born of an inner sense wholly separated from the accurate perception of a scientist. Part of this ideal is the unceasing search after a larger abstract truth than a scientific investigation permits of, a truth based upon a reasoned faith derived from a contemplation of life more than ordinarily well perceived. This is literature, dealing with those things into which science cannot go. But to this "poetic" thought, Osler adds practical application which would not occur to the poet. Here Osler's feet are solidly on the ground, though his head may be in the clouds; and his effusions take the form of advice to others beneath him in the climb (Osler, 1931):

> At the outset do not be worried about the big question—Truth. It is a very simple matter if each one of you starts with the desire to get as much as possible. No human being is constituted to know the truth, the whole truth, and nothing but the truth; and the best of men must be content with fragments. . . . In this unsatisfied quest the attitude of mind, the desire, the thirst . . . the fervent longing are the be-all and the end-all.

Pedagogical Essays.

So far it has been shown that Sir William Osler's biographical essays show his literary qualities working with his historical perspective, and his inspirational essays demonstrate a facility for "pure" literature with a practical application. In his pedagogical essays he deals with arguments in support of ideas in medical education. This was his important contribution to medicine: he wanted his epitaph to read: "Here lies the one who admitted students to the wards." Although these essays once again show his brilliant literary style in addition to his ideas on teaching medicine, they are not as important to the present study as are the biographical and inspirational essays or the literary investigations. However, "The Old Humanities and the New Science" (Osler, 1920), "Doctor and Nurse", "Teacher and Student", "Teaching and Thinking" (these three are in "Aequanimitas") and the "Licence to Practise" (Osler, 1889) are worth at least brief treatment.

His presidential address before the Classical Association in 1919, "The Old Humanities and the New Science", compares old and new ways of thought, using the medical and premedical curricula to illustrate his points. Here his ideas are established by historical observation, whereas in "The Licence to Practise", dealing with whether colleges, the State, or the profession should decide the matter of licensing, Osler uses an ethical and humanistic reasoning. Presenting opinions for the betterment of the race, all these essays are, in their broader sense, of value to the lay mind as well as to the profession. The spirit of the search for knowledge has become universal, and in this light "The Old Humanities and the New Science" takes on a significance for everyone who would get the most from his intellectual life. Pointing out as it does the absolute necessity of a proper balance between what Huxley chooses to call culture and a study of the nature of the physical cosmos, it compels the attention of any serious student of Osler's ideas of the relationship between the two.

Too, professional ethics, medical education and relationships between doctor and patient are of universal concern, for the State must safeguard its citizens. But it is not in this sphere that the literary value of these pedagogical essays lies. It is in the quality of Osler's doctrine, his vigorous observation, which forms the bases of his works, upon the human philosophy involved in the process of education. Because the ideas are, at bottom, of a personal nature, we again have arguments in support of subjective material. While they deal with Osler's philosophy of medical education, they are universal in their application to any teacher-student relationship. The dominant theme, here and in other of Sir William's writings, is: Education is a lifelong process. Teachers are not masters but simply advanced students, making available to younger students the fruits of their years of labour.

Both in essence and form this material is literary. It expresses, not what invariably and incontestably is, not a great cosmic truth, but what ought to be, what could be, if circumstances were properly made to suit. It is an expression of subjective reflection, the result of Osler's keen observations of nature—a result which is not a record but an interpretation. These ideas are conceived in wisdom and executed with clarity and vigour. As truly literature as are Milton's "Of Education" and parts of "Democracy and Education" by John Dewey, the American philosopher, Sir William's pedagogical writings are personal observations, thus subjectively realized, dealing with ideas rather than things; they are interpretations of things. Therefore they are criticisms of life.

Literary Investigations.

Osler's literary investigations are of interest to us, first because some of them are "literary" in the usual meaning of the term, such as this one on "The 'Phthisiologia' of Richard Morton, M.D." (Osler, 1904), which begins:

> August 22, 1662—Black Bartholomew's Day, as it has been called—brought sorrow and sadness to many English homes. The enforcement of the Act of Uniformity called for subscription to the Thirty-nine Articles, and enforced the use by all clergymen of the Book of Common Prayer. Among those ejected for refusal to subscribe—2,000 in number, it is said—was a young man, aged twenty-five, the Vicar of Kinver, in Staffordshire, Richard Morton by name.

As in "Michael Servetus" and "Fracastorius", Osler is here at his literary or dramatic best, opening a paper

with a colourful picture. And we have another instance of his unerring eye for historical priorities—Morton's "Phthisiologia" is one of the treatises on pulmonary consumption.

However, these investigations are being discussed because all of them deal in a scholarly way with books. Osler often delved into literature and history for their own sake; and his early medical bibliography throws light upon literary works of early authors as much as do special bibliographical or philological or historical investigations of any sort. Two of Sir William's best known investigations into matters of literature are the *"Bibliotheca Osleriana"* and "Creators, Transmutors, and Transmitters as Illustrated by Shakespeare, Bacon and Burton" (Osler, 1939). In the latter essay, read in 1916 at the Shakespeare Tercentenary Exhibition at the Bodleian, Osler speaks as a lover of good literature; thus, rather than a medical, it is a literary essay in that it introduces a new critical idea, original with Osler. It is developed, not by quotations illustrating the ownership of the idea by earlier critics, but by quotations from the works he speaks of. This is subjective material, derived from Osler's own contemplation and appealing to the inner sense of all his hearers. Shakespeare is the "creator" in the essay, Bacon the first great "transmuter" and Burton the last great "transmitter". Osler himself could be fitted into either of these latter categories: consider both the transmutation of nature's laws into human applications, as in his inspirational lay sermons and scientific essays, and the transmission of human thoughts in the abundance of quotations in all his writings, even strictly medical works.

Bibliography was much more to Osler than a "recreation", as listed in "Who's Who". As his colleague Dr. W. H. Welch (1927) has written:

> No small part of Osler's broadly liberal culture came from studies in medical history, biography and bibliography, which almost inevitably led far afield into the realms of classical and general literature and of social, political and philosophical history.

The *"Bibliotheca Osleriana"* (Osler, 1929), based on his own enormous medical library, filled with works in related fields, is a summary, so to speak, of all his work of a bibliographical nature. William Osler's works in the science of literature were prepared with the same care, the same depth of research, the same broad background as were his many contributions to the literature of science. Years of intense interest in books and bibliography led to his building an exceptionally fine library, a monument to which is the *"Bibliotheca"*. His introduction tells a delightful story, worth retelling once again, about a copy of Schmidt's *"Shakespeare-Lexicon"*, received from Berlin in 1875, when Osler was living in Montreal with a Mr. King:

> I looked at it hurriedly, but with much anticipatory pleasure. On my return to the house Mr. King, who had just come in, was sitting by the fire and greeted me in his cheery way with, "What's that you've got?" "Something that will rejoice your heart", I said, and deposited the work in his lap. The shock of the realization of a life-long dream, a complete concordance of Shakespeare, seemed to daze the old man. He had no further interest in me and not a word did he say. I never got it back! For months he avoided me, but helping him one day on the stairs, my manner showed that Schmidt was forgotten, and he never referred to it again. The work went to McGill College with his Shakespeare collection. When in the Library in 1910, I asked for the first edition of Schmidt and was glad to see my book again after thirty-five years. This story is written on the fly-leaf (cf. no. 5451) as a warning to bibliomaniacs!

Interrupted by World War I, Osler's *catalogue raisonne* was completed by Lady Osler after Sir William's death, with R. H. Hill, W. W. Francis and Archibald Malloch as editors. The work is divided into eight sections—"Prima" (a chronological bio-bibliographical account of the evolution of science, including medicine), "Secunda" (men whose contributions are not quite as notable as those in "Prima"), "Litteraria" (literary works by doctors and books dealing in a general way with doctors), "Historica", "Biographica", "Bibliographica", "Incunabula", and "Manuscripts". The volume contains 7787 entries. Two citations will show the "essay" flavour pervading even Osler's annotations to many of the entries. Under Oliver Wendell Holmes's "The Guardian Angel" (Item Number 4950):

> The New England doctor has been well drawn by Holmes in this novel. We are sorry not to have more of Dr. Lemuel Hurlbut, on whose pilulæ compositæ and sal polychrest five generations of Oxbow villagers had thriven. . . . The doctor in American fiction is strong only in New England, where he has reached a position difficult to match elsewhere. . . .

And of George Eliot's "Middlemarch" (Item Number 4770):

> Ask the opinion of a dozen medical men upon the novel in which the doctor is best described, and the majority will say "Middlemarch". Lydgate is at once an example and a warning. He illustrates an attempt to break tradition and custom in a provincial town by doing general practice and yet not dispensing drugs. . . . The warning in his case is plain—not to marry a fool with a pretty face! We follow his wrecked career with pathetic interest. An unmitigated calamity, his marriage ruined his intellectual life in a soul-wasting struggle with worldly annoyances. . . .

Again and again in dipping into the book one may find abundant illustration of Osler's own ideas in bibliography (Item Number 5526, taken from the *Veterinary Review*, Volume II, 1918):

> Not naturally dry, bibliography is too often made so by faulty treatment. What more arid than long lists of titles. . . . What more fascinating, on the other hand, than the story of the book as part of the life of the man who wrote it—the bio-bibliography.

The *"Bibliotheca"* furnishes splendid evidence of the wide background underlying Osler's various literary researches. It gives numerous examples of his critical abilities, and shows at the same time the unbelievable extent of his reading. Such a breadth of learning is, of course, necessary to the profitable carrying on of such literary investigations as Osler's, whether concerned with medicine or not. Even so, the vast knowledge requisite to a proper and significant study of bibliography is surprising when found in a man burdened with so many duties as this busy physician.

Among the group of essays concerned more or less with technical aspects of literary scholarship are "Physic and Physician as Depicted in Plato", "Books and Men", studies on Browne and Burton, and "The Earliest Printed Medical Books". The last, showing Sir William's grasp of medical *incunabula*, was given on his being elected president of the Bibliographical Society. It deals with the influence of printing from its beginnings until 1480 upon the art of medicine—a period "of greater typographical than scientific interest".

In the Plato essay Osler (1930) quotes in full one of the most celebrated passages with medical interest "in which Socrates professes the art of a midwife practising on the souls of men when they are in labour, and diagnosing their condition, whether pregnant with truth or with some 'darling folly'". Sir William himself went in for striking metaphors, as this one from "Books and Men" (Osler, 1930):

> To study the phenomena of disease without books is to sail an uncharted sea, while to study books without patients is not to go to sea at all.

Finally, one may be allowed two more quotations from Osler, these from "The First Printed Documents Relating to Modern Surgical Anæsthesia" (Osler, 1917). On the presentation of W. T. G. Morton's original papers to the Royal Society of Medicine, Osler began:

> Although the idea of producing insensibility to pain during a cutting operation is mentioned in the Book of Genesis (2.21) and the word anæsthesia first occurs in Plato and was used by Dioscorides, controversy has raged over who introduced anæsthesia. Which illustrates the absence of true historical perspective and a failure to realize just what priority means in case of a great discovery.

Although Dioscorides, Pliny, Hiotho the Chinese, Davy, Hickman and others knew of or used vapours to make

patients insensible, no one man forced the acceptance of one specific method or influenced surgical practice. Morton, a Massachusetts dentist, demonstrated in 1846 the simplicity and safety of ether, and to him credit goes for the development of surgical anæsthesia into a world-wide procedure. Thus Osler's axiom:

> He becomes the true discoverer who establishes the truth: and the sign of the truth is the general acceptance. . . . In science the credit goes to the man who convinces the world, not to the man to whom the idea first occurs.

Conclusion.

In this hasty survey of the writings of Sir William Osler there has been but small opportunity to dwell on his style, called by Christopher Morley "exquisite prose" and unfailingly praised by reviewers of his books. Influenced by his wide reading, clear and simple and tempered by unaffected grace, his style enabled him also to say much in a few words. In two sentences he sums up the failure of Greek science to progress further than it did (Osler, 1931):

> Man can do a great deal by observation and thinking, but with them alone he cannot unravel the mysteries of Nature. Had it been possible, the Greeks would have done it; and could Plato and Aristotle have grasped the value of experiment in the progress of human knowledge, the course of European history might have been very different.

Having accepted the idea that a definition of literature rests upon content more particularly than upon form, but that significant literature must be well built as well as deeply founded, one may arrive at an estimate of Osler's writings. The biographical, inspirational and pedagogical essays, judged by content, are literary in character; and of these the first makes a genuine contribution to medical history. The literary investigations, adding to our knowledge of the various periods into which Osler delved, are concerned in a scholarly way with literature and are valuable to students of philology and bibliography. Also, judged by form, all of Osler's works possess a unity and charm of style that places them among the best didactic essays of our day.

Bibliography.

Anderson, G. K., and Walton, E. L. (1939), editors, "This Generation", Chicago.

Chatard, J. A. (1920), "Osler and the Book and Journal Club", in "Sir William Osler, Bart.", Baltimore.

Cushing, H. (1925), "The Life of Sir William Osler", Oxford.

Morley, C. (1921), editor, "Modern Essays", New York.

Osler, W. (1889), "The Licence to Practise", *Maryland Medical Journal*, Volume XXI, page 61; reprinted in *The Journal of the American Medical Association*, Volume XII, page 649.

——— (1904*a*) "Science and Immortality", Boston.

——— (1904*b*), "The 'Phthisiologia' of Richard Morton", *Medical Library and Historical Journal*, Volume II, page 1.

——— (1908*a*), "An Alabama Student and Other Biographical Essays", Oxford.

——— (1908*b*) "Thomas Linacre", Cambridge.

——— (1909), "Michael Servetus", London.

——— (1917) "The First Printed Documents Relating to Modern Surgical Anæsthesia", *Annals of Medical History*, Volume I, page 329.

——— (1920), "The Old Humanities and the New Science", Boston.

——— (1926) "A Way of Life", New York.

——— (1929) *"Bibliotheca Osleriana"*, Oxford.

——— (1930) "Aequanimitas, with Other Addresses to Medical Students, Nurses and Practitioners of Medicine", Second Edition, Philadelphia.

——— (1931) "The Student Life and Other Essays", Boston.

——— (1939) "Creators, Transmutors and Transmitters. As Illustrated by Shakespeare, Bacon and Burton", reprinted in the *Bulletin of the History of Medicine*, Volume VII, page 403.

Welch, W. H. (1927), foreword to "Bulletin of the International Association of Medical Museums", Montreal.

MODERN TRENDS IN DIPHTHERIA PROPHYLAXIS.[1]

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IT is with sincere regret that we present this paper, as our former colleague, the late Dr. C. W. Adey, from his wealth of experience had intended to review modern trends in immunization against diphtheria, tetanus and pertussis.

Just over twenty years ago, at the third session of the Australasian Medical Congress, held in Sydney, Adey (1929) discussed the preparation and testing of substances then employed for immunization against diphtheria.

Then at the fifth session, held in Adelaide in August, 1937, he presented a paper (Adey, 1938) dealing largely with the merits of the then recently introduced diphtheria prophylactic "A.P.T.". Now, in spite of further advances, the problems associated with immunization against diphtheria are not wholly solved.

Immunological Principles.

Immunization against diphtheria is directed against the specific soluble exotoxin produced by *Corynebacterium diphtheriæ* either *in vivo* or *in vitro*. The protection which we aim to achieve is therefore antitoxic in nature. Doubt has been raised (Murray, 1935) whether more than one toxin was concerned in some severe diphtheritic infections but it has since been shown (Mueller, 1941; Zinnemann, 1946) that the toxin from all types of *Corynebacterium diphtheriæ* is neutralized by commercial antitoxin.

An artificially induced passive immunity of short duration may be obtained by administering antitoxic sera, but this paper is solely concerned with the more durable active immunity provoked by injection of antigens. An antigen has been defined as any substance which, when introduced parenterally into the animal tissues, stimulates the production of an antibody, and which, when mixed with that antibody, reacts specifically with it in some observable way.

No substance exemplifies this definition of an antigen better than does diphtheria toxin. Appropriate doses introduced parenterally into animals stimulate the production of an antibody, namely, diphtheria antitoxin. Further, when toxin is mixed with antitoxin under suitable conditions in the test tube a specific observable reaction occurs, namely, the flocculation phenomenon of Ramon.

The amount of circulating antitoxin is the criterion used by laboratory workers and clinicians alike for determining susceptibility to diphtheria and for assessing the results of immunization procedures.

The Schick reaction, while not indicating a fixed antitoxin level, is a useful guide to the immunity to clinical diphtheria. The modern Schick reagent is a carefully standardized diluted toxin, which allows a roughly quantitative measure of the circulating antitoxin to be made. Generally speaking, the "Schick-positive" person has less than one one-hundredth of a unit of antitoxin per millilitre of blood. It is noteworthy that we cannot fix a level of antitoxin which secures certain protection, but persons with less than this amount of antitoxin are regarded as unprotected (Ipsen, 1946).

The factors involved in the response of the host to the injection of diphtheria antigens are complex and can be dealt with only briefly here. The response can best be followed by noting changes in the antitoxin content of the blood.

Titration of blood antitoxin can be made with reasonable accuracy, but the method involved is tedious. Its use, however, when this has been possible, has greatly extended our knowledge of the fundamental immunological prin-

[1] Read at a meeting of the Section of Public Health, Tuberculosis, Tropical Medicine and Industrial Medicine of the Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

ciples concerned, and it has led to the improvement of antigens and of methods for using them.

Some of these basic principles are shown in Figure I, which is taken from "The Principles and Practice of Diphtheria Immunization" by Tudor Lewis (1941). The figure brings out the following points.

1. The effect of the primary dose of antigen appears to be the stimulation of susceptible cells of the body so that they will be in a condition to produce antitoxin readily when a further antigenic stimulus is applied. Detectable antitoxin in the blood is the exception at this stage (curves PX and PY), following the use of most antigens—the so-called anamnesic state.

2. The better the antigen, the greater is the stimulation of the susceptible cells (curves PX and PY).

3. The response to the secondary dose is more spectacular (curves AX and BY). Easily titratable antitoxin appears in the blood and later usually falls to a steady level.

4. The time interval between the primary and secondary stimulus is important (compare curves AX and BY with curves CX and DY).

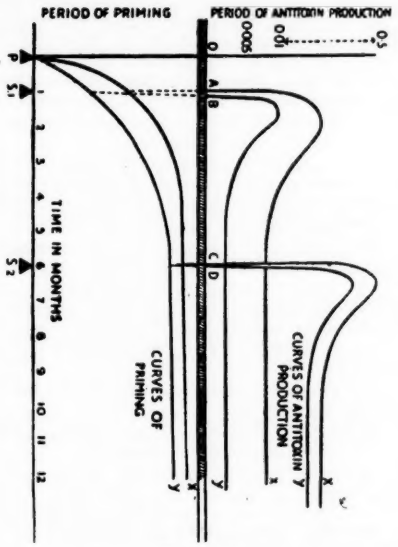

FIGURE I.

Diagram showing stages in antitoxin production after two injections of a diphtheria antigen (Tudor Lewis, 1941). The second injection is given (S.1) at one month, (S.2) at six months, after the first. The longer interval between the injections results in a higher titre as shown by curves CX and DY.

There are many technical difficulties in ensuring uniform efficiency of diphtheria antigens and the introduction of an international standard antigen is still awaited. Minimum standards of safety and potency of the different prophylactics are laid down in some countries which are satisfied by specified animal tests, but these do not ensure uniformity of antigenicity, and indeed they often tend to flatter inferior antigens.

In addition to the factors already discussed, that influence the antitoxic response to an antigen in animals and man, there are others that apply more particularly to humans. These include: (i) diphtheria experience and latent immunization, (ii) potential immunizability, and (iii) the amount of specific antigen injected and even the stimulus of the toxin used in Schick testing.

Stages in the Development of the Modern Diphtheria Prophylactic.

The increasing knowledge of these complexities must be borne in mind when one attempts to evaluate the various antigens evolved since von Behring introduced the first diphtheria prophylactic in 1913. His toxin-antitoxin mixture contained a slight excess of toxin over and above that needed to neutralize completely the antitoxin present in the mixture. It was found to be quite effective in use, high "Schick-negative" rates being reported after three injections. There were, however, hazards in its preparation, because not all sera and toxins combine firmly. Moreover, the presence of whole serum was not generally favoured.

Von Behring made a further great advance when he found that iodine modified toxin, so that it became non-toxic to animals whilst it retained its antigenic properties. To such a modified toxin the term toxoid was applied. Toxoid, when introduced parenterally into animals, stimulates the production of antitoxin.

Later, Glenny and Hopkins (1923) and Ramon (1923, 1924) showed that toxin could be converted to toxoid by exposing it to the action of formalin, and formol toxoid is still used extensively. For its preparation *Corynebacterium diphtheriæ* (Park 8 strain) is grown on the surface of liquid medium for eight to ten days. Formalin is added and the whole is kept at 37° C. to detoxicate. It is then filtered and tested for potency, antigenicity and lack of toxicity.

The antigenicity of formol toxoid tends to vary from batch to batch, and on account of the large amount of foreign protein it contains, allergic reactions tend to occur, especially in adults.

Before the immunization course of three doses is commenced, it is generally considered necessary to perform a skin sensitivity (Moloney) test. This involves the intradermal injection of 0·1 millilitre of diluted toxoid. If the individual proves to be both "Moloney positive" and "Schick positive", immunization with very small doses of formol toxoid may be attempted.

Four years after the introduction of formal toxoid Glenny and Pope (1927) described the preparation of floccules of toxoid and antitoxin ("T.A.F."). "T.A.F." has never been prepared in Australia, but in Great Britain it is claimed to be specially useful in the immunization of sensitive individuals, particularly adults. Three injections of "T.A.F." are recommended.

About the same time Glenny (1926) had shown that the antigenic value of formol toxoid was increased by the addition of alum, and this discovery was utilized in the immunization of horses. Then in 1931 Glenny and Barr described the precipitation of toxoid by potash alum, and in a later report Glenny and co-workers showed that the increased antigenic efficiency of alum-precipitated toxoid ("A.P.T.") was due to its slow absorption and elimination.

For the preparation of "A.P.T.", a sterile solution of alum is added to formol toxoid and a precipitate forms which carries down the antigenic fraction of the toxoid. The precipitate is washed and then suspended in saline. "A.P.T." is a purer product than formol toxoid.

Writing in 1941, Tudor Lewis (1941), after discussing the merits of the different prophylactics then available, concluded: "Examination of the results of Schick tests after the different diphtheria antigens reveals a great diversity of results not unexpected when the many factors influencing an antitoxic response are remembered." In that country (Britain) only one method, namely "A.P.T." administered by two injections, has given a consistently high Schick conversion rate.

Holt's Diphtheria Prophylactic, "P.T.A.P.".

Some workers, however, have hesitated to use "A.P.T." in children over the age of seven or eight years because some severe reactions have been reported following its use in the higher age groups. The recent announcement by Holt (1947) of a new prophylactic "P.T.A.P.", which is claimed to have definite advantages over "A.P.T.", including relative freedom from causing reactions, has therefore created widespread interest.

"P.T.A.P." (signifying purified toxoid adsorbed on aluminium phosphate) is prepared at the Commonwealth Serum Laboratories essentially as follows, the product finally containing 50 Lf. units per millilitre.

Corynebacterium diphtheriæ is grown on a simple casein hydrolysate medium, free from meat extracts. The toxin is treated with formalin, and the resultant toxoid is then purified by ultrafiltration followed by precipitation with ammonium sulphate and dialysis to remove non-specific proteins of metabolism and other impurities. It is next adsorbed on aluminium phosphate and kept for some months at room temperature to stabilize, when it is tested to ensure its antigenicity and lack of toxicity.

The technique of preparation is really far more exacting than this brief description might imply. Apart from the purity of the toxoid itself, a special feature of this product is the ease with which the amount of inert mineral carrier (aluminium phosphate) can be controlled. Holt and Bousfield consider the optimum amount of carrier to be 10 milligrammes per millilitre.

"P.T.A.P." then may be described as an accurately prepared prophylactic which, as regards its antigenicity, stability and freedom from causing reactions, has been claimed to be superior to "A.P.T." (Holt and Bousfield, 1949).

Route of Administration of Choice.

Regarding the route for administering "P.T.A.P.", Bousfield considers that intramuscular injection results in fewer reactions than does subcutaneous injection. Tudor Lewis (1941) and Parish (1948) both recommend the intramuscular injection of "A.P.T." for the same reason.

A further argument advanced for the use of the intramuscular route by Holt and Bousfield (1949) is that it confers definitely better immunity than does subcutaneous injection. This is of particular importance when it is not certain that the child will receive a second inoculation, and we believe that the intramuscular will ultimately become the route of choice in Australia.

P.T.A.P. as a Possible "One-dose" Diphtheria Prophylactic.

In spite of the distinctly promising results so far reported (Holt and Bousfield, 1949; Bousfield, 1949), a note of caution must be sounded against a possible tendency to assume that "P.T.A.P." is without doubt the long-looked-for "one-shot" diphtheria prophylactic. It may be, but we must await the results of further trials.

Shortly after the introduction of "A.P.T." it was widely predicted that the "one-shot" method had arrived, but it soon became apparent that results varied greatly (Adey, 1938), Bousfield (1937) being particularly critical of the method.

Now Holt and Bousfield (1949) report Schick-conversion rates of 97% to 99% following a single intramuscular injection of "P.T.A.P." with 94% of the recipients still "Schick-negative" after fifteen months or more. However, they have not yet suggested that the "one-shot" method should be generally adopted.

It is, of course, possible that an antigen such as "P.T.A.P.", which is potent and slowly absorbed, will provide the stimulus necessary for the production and maintenance of adequate antibody.

Dr. Cole's colleagues in the Victorian Health Department are now carrying out large-scale trials of the "one-dose" method in "Schick-positive" school children. As even the small amount of toxin used in post-inoculation Schick testing provides an additional stimulus tending to obscure results, the recipients are not being retested until the end of the present school year.

We already know that a single injection of "P.T.A.P." will result in nearly 100% of children being "Schick-negative" about one month later. It is the durability of this immunity that is in question, and we believe that until this is settled two well-spaced doses should be the routine procedure.

Age, Dosage and Reactions.

It would seem that even with such a relatively pure antigen as "P.T.A.P." allergic reactions may occur in older children and in adults, although to a lesser degree than with either "A.P.T." or formol toxoid.

There is general agreement that children up to the age of six years may be safely immunized without a preliminary sensitivity test. The optimum dosage in this group has not yet been determined, but we believe that the first dose should be the larger one. At present it is recommended that this should be 0·5 millilitre followed at least six weeks later by a second dose of 0·25 millilitre. There are, however, grounds for believing that smaller doses, perhaps 0·3 millilitre, followed by 0·2 millilitre, may be sufficient.

Regarding children over the age of six years, Holt (1949) has expressed the opinion that they should first be screened with the complete Schick test, which includes a control injection with heated toxin. This refinement to the ordinary Schick test allows susceptibility to diphtheria to be distinguished from allergy and is said to have now completely replaced the Moloney test in England (Parish, 1948). Holt advocates giving all except those proved to be allergic the same dosage as the younger children.

Dr. Forbes McKenzie is to give us the results of a large-scale trial of "P.T.A.P." in "Schick-positive" school children, and we shall be most interested to hear to what extent, if any, his experience supports Holt's view.

In conclusion we would pose the following questions which we consider need clarifying before immunization with "P.T.A.P." can be placed on a completely sound basis. What dose of "P.T.A.P." is sufficient to provide an adequate primary stimulus in the great bulk of children? Can this dose be given safely to all groups without preliminary screening? If the answer to the latter question is "No", what groups should be screened and how should this be done?

References.

Adey, C. W. (1929), "The Antigenic Value of Anatoxin", THE MEDICAL JOURNAL OF AUSTRALIA, Volume II, page 536.

——— (1938) "Certain Modern Agents for the Detection and Abolition of Susceptibility to Diphtheria", THE MEDICAL JOURNAL OF AUSTRALIA, Volume I, page 47.

Behring, E. von (1913), *"Über ein neus Diphtherieschutzmittel", Deutsche medizinische Wochenschrift*, Volume XXXIX, page 873.

Bousfield, G. (1937), "Diphtheria Immunisation: A Plea for the Immediate Abandonment or Control of 'One Shot' Treatment", *The Medical Officer*, Volume LVII, page 15.

——— (1947) "Clinical Trials of Diphtheria Toxoid Aluminium-Phosphate-Precipitated", *The Lancet*, Volume I, page 293.

——— (1947) "Holt's Diphtheria Toxoid (P.T.A.P.)", *The Lancet*, Volume II, page 867.

Glenny, A. T., and Barr, M. (1931), "The Precipitation of Diphtheria Toxoid by Potash Alum", *The Journal of Pathology and Bacteriology*, Volume XXXIV, page 131.

Glenny, A. T., and Hopkins, B. E. (1923), "Diphtheria Toxoid as an Immunizing Agent", *The British Journal of Experimental Pathology*, Volume IV, page 285.

Glenny, A. T., and Pope, C. G. (1927), "Diphtheria Toxoid-Antitoxin Floccules", *The Journal of Pathology and Bacteriology*, Volume XXX, page 587.

Glenny, A. T., Buttle, A. H., and Stevens, F. M. (1931), "Rate of Disappearance of Diphtheria Toxoid Injected into Rabbits and Guinea Pigs: Toxoid Precipitated with Alum", *The Journal of Pathology and Bacteriology*, Volume XXXIV, page 267.

Holt, L. B. (1947), "Purified Precipitated Diphtheria Toxoid of Constant Composition", *The Lancet*, Volume I, page 282.

——— (1948) "The Preparation of Purified and Concentrated Diphtheria Toxoid from a Semisynthetic Medium", *The British Journal of Experimental Pathology*, Volume XXIX, page 335.

——— (1949) personal communication.

Holt, L. B., and Bousfield, G. (1949), "P.T.A.P., The Present Position", *British Medical Journal*, Volume I, page 695.

Ipsen, J. (1946), "Circulating Antitoxin at the Onset of Diphtheria in 425 Patients", *Journal of Immunology*, Volume LIV, page 325.

Lewis, J. Tudor (1941), "The Principles and Practice of Diphtheria Immunization".

Mueller, J. H. (1941), "The Influence of Iron on the Production of Diphtheria Toxin", *Journal of Immunology*, Volume XLII, pages 342 and 353.

Murray, J. T. (1935), "The Relative Pathology for the Rabbit of Gravis, Mitis, and Intermediate Strains of Corynebacterium Diphtheriæ", *The British Journal of Experimental Pathology*, Volume XVI, page 384.

Parish, H. J. (1948), "Bacterial and Virus Diseases".

Ramon, M. G. (1923), *"Medicine experimentale—Sur le pouvoir floculant et sur les propriétés immunisantes d'une toxine diphtherique rendue anatoxique (anatoxine)", Comptes rendus des séances de l'Académie des sciences*, Volume CLXXVII, page 1338.

Zinnemann, K. (1946), "Neutralisation of C. Diphtheriæ Type Toxins with Standard Antitoxin, as Determined by Skin Reactions in Guinea Pigs", *The Journal of Pathology and Bacteriology*, Volume LVIII, page 43.

PURIFIED TOXOID ALUMINIUM PHOSPHATE ("P.T.A.P."): REPORT ON AUSTRALIAN FIELD TRIALS.

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IN April, 1949, the Commonwealth Serum Laboratories made available to the Department of Health, Victoria, a sufficient quantity of a diphtheria prophylactic known as "P.T.A.P.". Holt and Bousfield (1949) have published results of their experience with this material, and their reports were favourable; consequently it was agreed to conduct a field trial with this product.

To avoid too many variable factors and after consultation with the late Dr. Charles Adey, of the Commonwealth Serum Laboratories, the following routine was agreed upon: (i) All children would be Schick-tested without a control. (ii) The trial was to be limited to those definitely "Schick-positive" and not previously inoculated. (iii) The dosage was to be first dose 0·5 millilitre, and second dose 0·25 millilitre, given subcutaneously into the upper part of the left arm and right arm in that order. (iv) The intervals between doses were to be six weeks. (v) The post-Schick test with a control was to be carried out eight weeks after the second injection.

The First Injection.

Some 4500 children presented for Schick testing; of these the finding in 2500 was negative, in 1650 positive, and in 337 the reaction was marked as "doubtful".

Although main interest lay in the "Schick-positive" subjects, every child reacting in any way to the toxin (and this would include some protein and/or toxoid sensitive ones—that is, with combined reactions) was given an injection of "P.T.A.P.", 0·5 millilitre, subcutaneously into the left deltoid region.

Observations on the Practical Use of "P.T.A.P.".

The material is a thin fluid containing light white flocculated particles. It is easy to use; there is no gumming of syringes or blocking of needles.

Some children complained of a stinging feeling immediately after the injection. It seems that if any "P.T.A.P." is injected into the skin itself it causes pain; a deep subcutaneous injection is not objected to in most cases.

A number of children, mostly girls about twelve to fourteen years of age, experienced frontal headache, epigastric pain and faintness after the injection. The impression gained was that this reaction was mostly psychological. In a few instances a small injection of adrenaline was given, but in no case was the child unable to continue at school.

By inquiry from head teachers and parents it was discovered that a small number of true local and general reactions had occurred. All these children were visited by a medical officer. A severe reaction was accepted if it was necessary to keep the child away from school. These reactions will be discussed in detail later. At this stage it was decided that it would be an advantage to reduce the first dose to 0·25 millilitre, and to make the second dose 0·5 millilitre, unless contraindicated by a severe reaction after the first dose. In these cases the second dose could be reduced to 0·25 millilitre or omitted.

The Second Injection.

Six weeks after the first injection a second injection of "P.T.A.P." was given subcutaneously into the deltoid region of the right arm.

Prior to the giving of this injection an inquiry was made to see if the child had experienced a reaction to the first dose. Each answer was considered on its merits. In a very few cases the second injection was reduced in quantity or withheld.

Concerning this injection it was observed that the children did not complain as much as they did after the first dose. The transient faintness, frontal headache and epigastric pain previously remarked in some girls were not apparent this time. It appeared possible that the children and the doctors were gaining confidence in the product being used.

The Post-Schick Test and the Control.

The post-Schick test was carried out eight weeks after the second injection; however, a few children who had missed the first or second round were collected and tested. Some 1500 children attended. Many and varied reactions were seen, but in this series in only one case was anything like a Schick reaction observed, even when as small a dose of "P.T.A.P." as 0·25 millilitre had been given.

A point worth recording on technique is that it is necessary when repeating Schick tests to avoid the area used for the previous Schick reaction—that is, to use the other arm. Some reactions can be seen as a faint pigmentation of the skin as long as four months after a Schick test, and this pigmentation can be reactivated by further injections in the same spot.

The Schick toxin was shown to be potent, as a few children not inoculated in any way were also tested; these children gave typical "Schick-positive" responses.

It was not possible to estimate the minimum time to obtain a conversion from "Schick-positive" to "Schick-negative". The shortest interval in this series was eight weeks after a single injection.

"P.T.A.P." Inoculation Reactions.

Before we consider the practical results of the use of this prophylactic it is necessary to return to a consideration of the true reactions noted, so that an answer can be given to the question whether this material is safe to use under ordinary conditions.

Apart from this series, other doctors in the Victorian Department of Health have used "P.T.A.P."; in all some 3000 children have received one or more injections. No alarming reactions have been reported.

In this trial a severe reaction was noted and investigated if the child was away from school after the injection. In addition, a general survey of the schools was made in order to gain an impression of the "discomfort" produced by "P.T.A.P.". The discomfort experienced was not undue. In most cases a small brawny swelling could be found at the site of the injection, surrounded by an erythematous area of local extent. The erythema fades in a day or two, and the swelling subsides slowly, leaving a nodule beneath the skin in the same way as "A.P.T.". After six weeks this nodule has practically disappeared or may be felt as a grain of wheat or a small pea. This is much less severe than, and does not persist as long as, the nodule left after "A.P.T.", which is usually quite hard and may be tender for over six weeks. In no case did the "P.T.A.P." nodule break down or become fluctuant.

Tabulated "P.T.A.P." Reactions.

Nearly 2000 children were inoculated in this field trial; as far as could be ascertained, only eight were kept at home because of inoculation reactions (see Table I).

School Reports Concerning Reactions.

The headmasters as a whole were not worried by the inoculation reactions; they and their staff gave every assistance during the doctor's visits to treat the children. It was found that violent exercise after injections aggravated the reactions and it is inadvisable.

General Discussion of the Reactions.

It is difficult to avoid some reaction to inoculations; the severe reactors are said to develop high antitoxin titres. With two exceptions the severe reactions occurred after

[1] Read at a meeting of the Section of Public Health, Tuberculosis, Tropical Medicine and Industrial Medicine of the Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

TABLE I.

Severe "P.T.A.P." Reactions, that is, Sufficient to keep the Child Away from School.

Sex.	Age. (Years.)	Past History.	Result of First Schick Test.	Reaction after "P.T.A.P." 0·5 Millilitre.	Reaction after "P.T.A.P." 0·25 Millilitre.	Remarks on Result of Final Schick Test and Control.
M.	15	P.I.	±	Arm swollen, two days in bed.	Not given.	Negative. Protein sensit ve.
M.	14	P.I.	+	Played football after the injection, arms painful, away from school.	No reaction.	Negative. Inoculation reactions aggravated by exercise.
M.	15	P.I.	+			
F.	14	P.I.	+	Arm swollen, two days in bed.	No reaction.	Negative.
F.	12	N.P.I.	+	Swollen arm, two days in bed.	Not given.	Not done.
F.	10	N.P.I.	+	Arm stiff and swollen.	Refused.	Not done. Parent exaggerated reaction.
M.	16	Moloney *plus* N.P.I.	+	No reaction.	Arm swollen, two days in bed.	Negative.
F.	9	N.PI	+++	No reaction.	Arm swollen, local blistering.	Pseudo - negative. Control showed protein sensitivity.

P.I. = Previously inoculated; N.P.I. = Not previously inoculated.

the first dose of 0·5 millilitre. In the other two the severe reaction was after the second dose of 0·25 millilitre. There seems to be no way of anticipating such happenings. Two children known to have suffered from diphtheria also experienced reactions. In large-scale campaigns it is impossible to consider every individual's possible idiosyncrasies. Some children known to suffer with allergic reactions were given "P.T.A.P."; one asthmatic and one liable to urticaria stood the full course without any disability. Until further information is available the safe rule is to give a small injection at first and a full dose at the second round unless contraindicated by circumstances. A reduced dose is advisable if the Schick reaction is unusually pronounced.

For the present it can be repeated that over 3000 children have received "P.T.A.P." without untoward results.

TABLE II.

Observer.	Number of Subjects.	First Dose. (Millilitre.)	Second Dose. (Millilitre.)	Result of Final Schick Test.
Group A. Children "Schick-positive", Not Previously Inoculated.				
Mackenzie and Holder.	918	0·5	0·25	Practically 100% negative.
		or		
		0·25	0·5	One doubtful positive.
Group B. Children "Schick-positive", Previously Inoculated.				
Mackenzie and Holder.	307	0·5	0·25	100% negative.
Crowe	165	0·25	0·5	100% negative (Schick test six months after final injection).
Crowe	164	0·25	0·5	One positive, remainder negative.
Total ..	1554	Total dosage, 0·75 millilitre, in two doses at six weeks' interval.		99·8% negative.

Results of the Field Trial.

If we exclude 337 initially "Schick-doubtful" children, information is available concerning Schick conversion in 1554 "Schick-positive" children (Table II). Some grouping is necessary because of differences between the children in inoculation history *et cetera*.

In addition to the above some 300-odd "Schick-doubtful" children were treated and tested; these all converted to a "Schick-negative" state. A more important group is a smaller one the members of which received only one dose (Table III). After one injection of "P.T.A.P." 96·7% of the individuals converted to a "Schick-negative" state. This result is certainly superior to that obtainable with any other prophylactic available in Australia, when used in these small quantities. Further tests are being carried out to determine the efficacy of "one-shot" prophylaxis with "P.T.A.P.".

Duration of Immunity.

Some of the children in the above series were Schick-tested six months after their treatment. It was found that not one child among 1241 tested who had received two injections of purified toxoid aluminium phosphate was "Schick-positive" six to nine months later.

Dosage Requirement and Injection Technique.

The use of a priming dose of an antigen, followed later by another dose of the same antigen, has been shown to produce the best antitoxin response. This work is practically a basic principle in immunological technique (A. T. Glenny, quoted by Tudor Lewis, 1941). For this reason, unless the community has been primed by natural infection in subclinical doses, it seems likely that "one-shot" prophylaxis may lead to variable results. Theoretically, if diphtheria is controlled by immunization, the stimulus of natural priming with antigens would be absent.

TABLE III.

Children "Schick-positive", Not Previously Inoculated.

Observer.	Number.	Dosage. (Millilitre.)	Result of Post-Schick Test.		
			Negative.	Positive.	Doubtful.
Mackenzie and Holder.	50	0·5	45	3	2
Crowe	123	0·5	120	1	2
Crowe	120	0·3	118	0	2
Mackenzie and Holder.	18	0·25	18	0	0
Total ..	311	0·25–0·5 millilitre, one dose	301	4	6
			96·7% conversion		

In this series there is an indication of failure with one dose—that is, 96·7% conversion in 300-odd, as against 99·8% converted to a "Schick-negative" state in the larger group of 1550. (See Tables II and III.)

From these considerations it seems that two doses are necessary. An estimate of the quantity required may be arrived at from the figures quoted above. On present indications 0·5 millilitre is not sufficient, but 0·75 millilitre is almost 100% satisfactory. A convenient splitting of the dosage is 0·25 millilitre and 0·5 millilitre.

The interval between the doses was fixed in this trial as six weeks. A longer interval may give better results, but from other work it must be accepted that an interval of four weeks is the minimum period.

All the injections have been given subcutaneously. Holt and Bousfield (1949) have worked with intramuscular injections and have claimed better results. In this trial the subcutaneous method of injection generally adopted with "A.P.T." and combined prophylactics has been followed with "P.T.A.P.". In some ways a subcutaneous injection is easier, and it seems to be safer when fine needles are used. Finally, the slower absorption factor postulated as an advantage with precipitated and adsorbed toxoids may be eliminated by intramuscular use.[1]

Practical Use of "P.T.A.P.".

From the above discussion the following method of using "P.T.A.P." is recommended:

For infants, a dose of 0·25 millilitre is given subcutaneously, followed in six weeks by 0·5 millilitre in the other arm.

For school children up to the age of fifteen years but not sixteen years, a dosage of 0·25 millilitre and 0·5 millilitre, the second dose being reduced to 0·25 millilitre if the larger dose is contraindicated.

For adults, students *et cetera*, who have mostly been previously inoculated, a Schick test should be performed, and one should then proceed cautiously with 0·25 millilitre doses.

Boosting doses should be given as required to previously inoculated children joining school, or to convey quick protection when an epidemic is likely. A dose of 0·25 millilitre is used, with a Schick test when convenient at a later date and repetition of the dose if necessary.

Conclusion.

An attempt may be made now to assess "P.T.A.P." as follows:

1. It is a safe diphtheria prophylactic.

2. In two doses, amounting in all to 0·75 millilitre, it has given a Schick-conversion rate of 99·8% in 1500-odd children.

3. Its effectiveness in controlling diphtheria will take time to prove. In this series no cases of diphtheria have been reported in the inoculated. Two cases of diphtheria, one in a man aged forty years, and the other in a girl not tested or treated, have been notified recently in the Prahran municipality. In other words, a virulent diphtheria organism is present in the community, but the immunization procedure with "P.T.A.P." has not broken down.

Summary.

A field trial has been carried out by the Department of Health, Victoria, with purified toxoid aluminium phosphate ("P.T.A.P.") prepared by the Commonwealth Serum Laboratories.

Some 3000 children have been inoculated with one or more doses without untoward results. "P.T.A.P." can be considered a safe diphtheria prophylactic.

"P.T.A.P." is easy to use, but like other toxoids it will give rise to reactions in the older age groups. In this trial only four children in every 1000 had reactions which necessitated bed rest.

Compared with the prophylactics in general use in Australia—that is, alum precipitated toxoid ("A.P.T.") and formol toxoid ("F.T.")—it can be said that "P.T.A.P." does not cause local reactions as severe as "A.P.T.", and "P.T.A.P." will not necessitate as many injections as are required with "F.T.".

The general over-all conversion rate to a "Schick-negative" state in 1550 children who received 0·75 millilitre of "P.T.A.P." divided into two doses was 99·8%.

Dosage recommended is as follows (interval between doses four to six weeks): infants—first dose 0·25 millilitre given subcutaneously, second dose 0·5 millilitre; school children—first dose 0·25 millilitre, second dose 0·5 millilitre, unless contraindicated, when the dose should be reduced to 0·25 millilitre or omitted; adults, students *et cetera* (mostly previously inoculated)—perform Schick test and proceed cautiously by giving 0·25 millilitre doses to the "Schick-positive" subjects. Boosting doses are given as required for previously inoculated children joining school; a dose of 0·25 millilitre is given in one injection.

Schick tests are not necessary as a rule except when one is dealing with special groups mostly previously inoculated.

Acknowledgements.

All the Schick toxin and the purified toxoid used in this trial were manufactured and supplied by the Commonwealth Serum Laboratories. The trial was initiated by the late Dr. Charles Adey and was carried out by the Department of Health, Victoria, in conjunction with Dr. J. P. Major, the medical officer of health of the City of Prahran, and the Prahran city health inspectors and nursing sisters. The enthusiasm of all concerned in this work has been clouded by the untimely death of Dr. Adey.

References.

Holt, L. B., and Bousfield, G. (1949), "P.T.A.P., the Present Position", *British Medical Journal*, Volume I, page 695.

Lewis, J. Tudor (1941), "The Principles and Practice of Diphtheria Immunization", Oxford University Press.

[1] Since the presentation of this paper Holt has published a monograph which presents an important challenge to the work of Glenny, quoted above. Holt's book, "Developments in Diphtheria Prophylaxis", 1950 (William Heinemann, London) should be consulted by all workers in the field of diphtheria immunization.

THE PATHOGENESIS OF ATHEROMA, WITH SPECIAL REFERENCE TO DISORDERED LIPOID METABOLISM.

By GEORGE V. HALL,
Sydney.

ATHEROMA is an arterial lesion characterized by a patchy thickening of the intima with underlying patches containing fatty yellow, degenerative, porridge-like material from which the disease derives its name (ἀθήρη, gruel). It occurs in arteries of all sizes, but is particularly common in the aorta and in certain of the smaller arteries which are poorly supported, most particularly the cerebral and coronary vessels.

There has always been a great deal of confusion regarding the terms atheroma and arteriosclerosis. The former is a patchy degenerative lesion of the intima as described above, whilst the latter is a diffuse lesion affecting the whole arterial tree, in which, as Muir states, "there is usually a combination of hypertrophic and fibrous changes in the arterial wall".

Arteriosclerosis in its characteristic form is accompanied by arterial hypertension, whilst there is little evidence that long-continued high blood pressure leads to atheroma.

By far the most important cause of coronary artery occlusion is atheroma with or without an added thrombus. Indeed, pathologists find that in 80% or more of fatal cases of coronary occlusion the occlusion is purely atheromatous and a clot is found in the artery only in the remaining minor percentage of cases.

Wright-Smith (1936), in an analysis of 495 cases of coronary obstruction, found at autopsy that thrombosis of the coronary artery occurred in only 45 cases, and even in these it did not cause immediate death in the majority of cases. This is a fact which could well be given more attention by clinicians.

The underlying pathological lesion in most cases of cerebral thrombosis and hæmorrhage is atheroma.

Atheroma may occur in other arteries, including the arteries of the limbs, giving rise to intermittent claudication, ischæmia and gangrene.

As the average expectancy of life is increasing, the magnitude of the clinical problems arising from the effects of atheroma continues to grow. But although atheroma

has usually been regarded as a degenerative process associated with advancing years, its incidence is apparently increasing in the earlier age groups. Thus large series of cases of coronary artery occlusion in young men in the American army have recently been reported. Yater, Traum, Spring Brown, Fitzgerald, Geisler and Wilcox (1948) reported 866 cases of coronary artery disease in men of the American army aged eighteen to thirty-nine years; 203 of these men were aged under thirty years. In all fatal cases extensive atheroma of the coronary vessels was present. Therefore, the importance of attempting to gain some knowledge of the ætiology of this lethal condition cannot be over-assessed. A knowledge of its ætiology is, of course, essential if we are to do anything to prevent or delay its onset or progress, or if possible to reverse processes which have already taken place.

A great deal of work has been done in an attempt to elucidate this great and important problem, but it is only recently that significant progress has been made.

Modern Views on Possible Ætiological Factors.

Broadly speaking, we have two generally accepted views regarding the ætiology of atheroma.

The first view is that atheroma is a degenerative process usually associated with advancing years. Boyd (1943) writes: "Atherosclerosis is a degenerative process associated with advancing years, which in one way seems as natural as the greying of the hair. It is the end of a song which is sung in the cradle." Clifford Allbutt (1915) remarks: "It cannot be supposed that the stealthy hours carry away no quantities of tissue, no quantities of energy." Certainly we know that the first traces of atheroma probably make their appearance in the average person at the age of about thirty years and increase in extent with increasing age; but we also know that in persons aged over eighty years there may be scarcely a trace of atheroma, whereas it may be present to a considerable extent in the very young.

Gavy (1949) found that in a series of over 300 patients aged seventy years or over, 10% had no trace of atheroma at autopsy.

The second view of the ætiology of atheroma is that heredity without any doubt plays an important part.

Mortensen (1925) in an analysis of 300 cases of atherosclerosis found a family history in 67·5%; and many of the remaining patients did not know the cause of death of their ancestors. Other workers elicited a family history of atheroma in 68% of cases. One patient, whose father had died of apoplexy and whose mother had died of cardiovascular renal disease, had nine brothers and sisters, all of whom had died of apoplexy, and he himself had already had a stroke.

Muir (1936) summarizes his discussion of the ætiology of atheroma as follows:

> The intima of arteries is prone to undergo degeneration, as is shown by the fatty change in young subjects, and this tendency increases in the later years of life and is still further intensified by a variety of conditions—toxic action, strain, abnormal metabolism etc.

An example of toxic action could be atheromatosis of younger people, which Boyd (1943) states may occur after an attack of one of the infectious fevers. He writes that it seems probable that these lipoid deposits may later be absorbed.

With regard to strain as a factor, it seems that local strain is likely to be more important than a generalized increase in arterial tension.

Thus aortic lesions are nearly always prominent at points which may be considered specially subject to strain, such as the bifurcation of the aorta and the sites of origin of intercostal and lumbar arteries. Wilens (1942) found that applications of cylindrical silver cuffs to the femoral and carotid arteries of rabbits, followed by cholesterol feeding, led to localization of lipoids in the intima at points of pressure.

On the other hand, Goldblatt (1934) has never seen atheroma of the aorta in hypertensive dogs.

It seems, therefore, that localized stress or strain may play a part in the production of atheromatous lesions, rather than a generalized increase in blood pressure.

Most of the significant progress made recently in our knowledge of the factors involved in atheroma has been along the lines of abnormal lipoid metabolism. This is not a new method of approach, as considerable interest has been shown in this aspect of the problem for some years past, particularly in America. However, brilliant experimental research, which has revolutionized ideas about fat metabolism and absorption, coupled with the clinical evidence we possess, has recently added weight to the concept that an instability of the plasma lipoid of transitory or persistent nature is related to the development of these lesions. It is suggested that disorders of lipoid metabolism and abnormalities of intracellular oxidation processes are the cause of these disturbances of the plasma colloids.

The essential lesion of atheroma is the accumulation in the intima of lipoid, mainly cholesterol and its esters. As to the significance of this, two views are held: (i) intimal degeneration is primary and deposition of lipoids secondary; (ii) the deposition of lipoid is the primary condition, intimal degeneration being secondary.

Of the lipoids, most attention has been devoted to cholesterol. From the results of experimental work it would appear that cholesterol is concerned with the transport of fatty acids to the cells for utilization. But if one subscribes to the cholesterol theory in the development of atheromatous lesions, one must also be interested in the transport of fatty acids in the body, because it is now thought that the unsaturated fatty acids especially compete for esterification with cholesterol as a vehicle for their transport.

The evidence for the cholesterol theory is both experimental and clinical. Atheromatous deposits in the aorta of rabbits have been produced by feeding them a diet rich in cholesterol. Leary (1935) succeeded in reproducing with remarkable exactness the lesions of human atherosclerosis in the coronary arteries of rabbits by feeding them with cholesterol for long periods. Other workers successfully produced generalized atheromatosis in the chicken by cholesterol feeding.

These results, of course, cannot provide grounds for the belief that human atheroma is related to a high cholesterol content of the diet or to hypercholesterolæmia. The normal blood cholesterol content of the rabbit is low and is much raised by the administration of cholesterol, whereas in man the normal level is high.

Boyd points out that experimental cholesterol atheroma cannot be produced easily in dogs and cats, so that there exists a sharp species difference in experimental animals. He holds that this may be partly due to the fact that the herbivorous rabbit is unable to metabolize cholesterol, whereas the carnivorous cat and dog possess this capacity.

It is conceivable that so-called "cholesterol families"—that is, families of whom several members may have a high serum cholesterol level and a tendency to the early development of atheromatous lesion—may have an inherited weakness in lipoid metabolism, which leads to persistent hypercholesterolæmia and the subsequent development of atheromatosis; that is, they may have a lipoid metabolism analogous to that of the rabbit.

The ingestion of much cholesterol by the normal human being will affect high blood levels only in the obese and when concomitantly a diet richer in fat is taken.

Turner and Steiner found that the serum cholesterol level of a subject tends to remain remarkably constant throughout the day, regardless of the taking of a breakfast rich in cholesterol—but they also concluded that the serum cholesterol level of patients with overt coronary arteriosclerosis was significantly higher than that of normal subjects of the same age group.

The clinical evidence in favour of the cholesterol theory is strong. The almost inevitable development of a fatty liver in most diabetics, as well as their pronounced tendency to vascular degeneration, seems to be related to

errors of fat metabolism, particularly the enforced transport hyperlipæmia. This transport hyperlipæmia is, of course, brought about by the mobilization of fat from the fat depots to replace carbohydrate which has become unavailable as a fuel. The vehicles of fatty acid transport are thought to be essentially cholesterol and the phospholipids.

Pronounced hyperlipæmia, sometimes associated with eruptive xanthomata in the skin, was common in severely diabetic subjects in the pre-insulin days, when diets poor in carbohydrate and rich in fat were taken—the vogue in the treatment of *diabetes mellitus*. These patients showed a pronounced tendency to early vascular degeneration.

Shivelhood (1948) reported a fatal case of coronary occlusion in a boy, aged twelve years, who had been a diabetic from the age of two years.

The second group of patients who clinically support the cholesterol theory are the cholesterol families, which have been mentioned above and which have been fully discussed by Boas, Parets and Adlersberg (1948).

The brilliant work of Rudolf Schoenheimer (1949), with his isotopic tagging of fat, has shown beyond doubt that, contrary to old beliefs that the fat in the depots was an inactive, inert tissue, the body fats are in a constant state of rapid flux. Schoenheimer writes:

> The fatty acids of the depot fat are to be regarded as being constantly transported in the form of fats or phosphatides to and from the organs, where fatty acids are temporarily liberated by rupture of ester linkages. When fat is absorbed, the acids of dietary origin merge with those from the depot, thereby forming a mixture indistinguishable as to origin. Part of the liberated acids are converted into others, while new ones are steadily formed by condensation of small molecules derived from other substances. Some of this pool of acids is degraded and some of it reenters ester linkages to regenerate fat which is transported back to the depots. All these complex reactions are so balanced that the total amount and structure of the fat mixture in depot, blood and organs remain constant.

If this is so, it is easy to understand how such a balance could be upset by abnormalities of fat absorption, transport, utilization or storage. An inherited weakness of fat metabolism or an acquired disorder, such as an uncontrolled diabetic condition, could do this. The remittent hyperlipæmia may well be a sinister factor in the deposit of lipoid in the intima of the blood vessel with the premature or accelerated development of atheroma.

Hueper (1944, 1945), by repeated injection of aqueous solutions of polyvinyl alcohol, methyl cellulose, pure citrus pectin and gum acacia, produced in the arterial intima of does, rabbits and rats lesions whose morphological appearance and distribution were typical of atheroma, except that the deposits were of the injected substance instead of lipoid material. The injected substances were all of high molecular weight.

Many other foreign substances of lower molecular weight may be maintained at high blood levels for long periods without deposition in the arterial intima. Hueper expressed the opinion that the "macromolecular" substances form a film at the plasma endothelium interface, producing anoxia of the intima with resultant pathological changes in the intima.

The Chylomicron Theory.

John R. Moreton (1948), working at the Joseph Edgar Tyrie Memorial Laboratory for Research on Arteriosclerosis, Salt Lake City, Utah, shortly afterwards put forth his chylomicron theory. He found that the lipid particles in the plasma in sustained hyperlipæmia of metabolic experimental origin were so large as to be readily visible in the dark-ground illumination microscope, and also that they were readily separated to the top in a lipoid layer by moderate centrifugation. This state of affairs in conditions which are known to predispose the subject to atheroma is in contrast to the state of affairs in normal plasma, wherein most of the lipid is stabilized in colloidal particles too small to be seen by dark-field illumination and not separated by even relatively high-speed centrifugation. Moreton also demonstrated that the lipoid particles which appear in normal plasma following absorption of fats from the intestine (that is, during alimentary hyperlipæmia) were also of large colloidal size, visible by dark-ground illumination and readily separated by centrifugation. From this observation he put forward the theory that atheroma in human beings might be due to the cumulative effect of many fatty meals over a lifetime, which had produced transient showers of large lipoidal particles in the plasma. He called these large lipoidal particles chylomicrons. He went on to point out that these large lipoid particles, passing from the lymph into the intima, incited the foreign-body response which is a characteristic histological feature of the origin and development of atherosclerosis. Moreton holds that triglycerides and fatty acids are rapidly absorbed from these particles, but cholesterol, which is difficult to absorb, remains and accumulates as the predominant residue in the intima. Particles which contain larger percentages of cholesterol than normal leave a larger residue and build up intimal lesions more rapidly.

Moreton's theory, then, goes far towards explaining low plasma cholesterol readings after a fatty meal, when the cholesterol content of the blood is really ten or twenty times greater than in the fasting state.

From the evidence available it seems that the cholesterol ester rather than free cholesterol acts like a macromolecular foreign body when out of its normal site and enmeshed within the wall of a blood vessel. Esterified cholesterol is normally present only in the liver, the intestinal mucosa and the blood plasma. Since the ester is at fault, not only cholesterol but also the other part of the ester, the fatty acid, is apparently important in the production of atheromatous lesions.

Although the total amount of chylomicrons after a meal is always in direct proportion to the quantity of fat digested, Setala (1948) observed that the metabolic rhythm of the visible lipoidal plasmatic aggregates—that is, the chylomicron curve—was characteristic for the individual and remained comparatively constant under the same external conditions. While in most persons there was a rapid increase of the chylomicrons after a fatty meal followed by an abrupt drop, in some persons one or more generally lower "after-peaks" were found.

The Chylomicron Curve as a Lipoid Tolerance Test.

This finding raises the question of the possibility of detecting subjects with a disordered lipoid metabolism by some type of lipoid tolerance test.

Setala's method of plotting the chylomicron curve is one possibility.

C. H. Becker, Jacob Meyer, and H. Necheles (1949) found that the chylomicron counts of young subjects reached a peak at two and a half to three hours and returned to fasting levels by the end of the fifth hour. The counts of an older group of subjects, on the other hand, did not reach their peak until eight to twelve hours, and they did not return to fasting levels until twenty-four hours had elapsed. In addition, the total number of chylomicrons was found to be consistently and considerably higher in the old than in the young group. These workers found that, particularly over the age of fifty years, chylomicronæmia is of greater intensity and is practically permanent. They also hold that oral administration of lipase or of a detergent with the fat meal reduced the hyperchylomicronæmia of older persons to practically the level of the earlier age group.

Leary's theory of transport of the ester by phagocytic cells has its arguments.

Gordon (1947), elaborating on this theory, held that atheroma was mainly a disease of the elastic arteries, because as they were filled only in systole and were partially emptied during the whole cardiac cycle, the current had a certain intermittency. He also pointed out that these arteries dilated with age, thereby slowing the blood flow. The lipophages were thereby able to move into the peripheral blood-stream and come in contact with the endothelium. Because of their lightness and relative inertness, they could be pushed into the intima by the blood pressure.

TABLE I.

Diet.

Meal.	Protein. (Grammes.)	Carbohydrates. (Grammes.)	Fat. (Grammes.)	Calories.	Thiamine. (Microgrammes.)	Riboflavin. (Microgrammes.)	Niacin. (Milligrammes.)	Iodine.	Lecithin.
Breakfast:									
180 grammes of rolled oats (cooked)	5	19	2	114	204	39	0·33	+	–
120 grammes of milk (skimmed)	4	6	1	42	96	432	0·24	+	+
1 average egg (poached)	6	—	5	79	60	170	0·05	–	++
40 grammes of wholegrain bread (100%)	4	19	1	79	112	60	0·131	+	–
5 grammes of butter	—	—	4	36	—	—	tr.	–	–
20 grammes of marmalade	—	14	—	58	4	4	0·01	–	–
240 grammes of coffee, skimmed milk (Soluble coffee)	8·5	12	2	84	96	432	0·24	+	–
	—	—	—	—	10	3	0·56	–	–
Morning tea:									
200 grammes of orange juice	—	20	—	80	80	30	0·20	–	–
Dinner:									
50 grammes of whiting or other white fish	14	—	4	90	30	30	2·52	++++	–
100 grammes of potato	2	19	1	85	99	38	1·08	+	–
100 grammes of carrots	1	9	—	45	70	60	0·50	++	–
100 grammes of string beans	2·5	7·5	—	42	80	100	0·60	–	–
120 grammmes of milk (junket)	4	6	1	42	96	432	0·24	++	–
150 grammes of apple (steamed)	—	22·5	—	96	40	20	0·20	–	–
Afternoon tea:									
60 grammes of milk tea	2	3	0·5	21	46	216	0·12	++	–
2 grammes of arrowroot biscuit	1	6	1	21	—	—	—	–	–
120 grammes of sugar (for day)	—	120	—	480	—	—	—	–	–
Tea:									
100 grammes of tomato	1	4	—	23	60	40	0·60	++	–
50 grammes of lettuce (green) salad	0·5	1·5	—	8	60	70	0·20	+++	–
100 grammes of asparagus	2	4	—	24	166	170	1·20	+++	–
40 grammes of wholegrain bread	4	19	1	79	112	60	0·131	+	–
5 grammes of butter	—	—	4	36	—	—	tr.	–	–
20 grammes of jam	—	14	—	—	2	4	0·03	–	–
100 grammes of banana	1	23	—	99	90	60	0·60	–	–
60 grammes of milk tea	2	3	0·5	21	48	216	0·12	++	–
Supper:									
240 grammes of "Milo" (on milk)	8·5	12	2	84	96	432	0·24	–	–
Total content	73	362	30	1868	1857	3098	10·142		

This process is held to be easier also in the elastic arteries because the internal elastic lamellæ are less well developed or do not exist.

Comment.

The points to be appreciated are these: (i) It is the ester which is significant, and the deposition does not depend entirely on high plasma levels of free cholesterol. (ii) Excessive transport of fatty acids, whether from excess ingestion of fats, mobilization from fat stores or polymerization of breakdown products with food moieties, should be avoided in the human candidate for vascular degeneration.

What causes the ester to drop out or be deposited in the intima of the blood vessel is still a moot point. Electrical changes of the molecule in its colloidal state may play a part in the abnormal deposition. Hueper states that quantitative and qualitative disturbances in the equilibrium of the plasma lipoids affect the degree and stability of their colloidal dispersion and produce a tendency towards the formation of coarse aggregates and their precipitation on the arterial intima.

Preventive and therapeutic management of atherosclerosis resulting from metabolic and hæmatic disorders is aimed at correcting these disorders as well as at removing the lipoid deposits in the arterial walls.

Methods Suggested for Preventive and Therapeutic Management of Atherosclerosis.

The following are suggested methods for the prevention and treatment of atherosclerosis.

1. Stimulate the oxidation processes of the body by administering thyreoid and the oxytrophic factors of the vitamin *B* complex.

2. Control lipoid and cholesterol metabolism, reducing drastically the dietary intake of cholesterol and fat and giving adequate amounts of lipotropic factors of vitamin *B* complex (namely, choline, inositol and pyridoxine).

3. Stabilize the colloidal equilibrium of plasma lipoids through a sufficient dietary intake of proteins and phospholipids (plasma proteins, lethicin and other phospholipids tend to maintain the plasma lipoids in a state of supersaturated solution in the serum and a continual degree of dispersion of colloid lipid particles); and mobilize arterial lipoid deposits through the action of the lipotropic vitamins and the detergent action of phospholipids.

Suggested Lines of Research.

Further lines of research which could be followed are suggested by McArthur's idea that the difference in the species of the herbivorous animals, which cannot metabolize cholesterol, and the omnivorous animals, which can, may be in the enzyme system in the arterial wall. If this system is inadequate to deal with the lipoid presented to it, the latter cannot fail to accumulate in the intima. Various factors may influence the enzyme-splitting system, including age, heredity and mechanical strain.

The esterase mechanism may be under chemical or hormonal control. This is suggested by the fact that the cholesterolosis of the aorta produced in rabbits by feeding them cholesterol is prevented by the administration not only of thyreoid gland, but also of iodine. Thyreoidectomy may cause a pronounced increase in the blood cholesterol level, and it is known to be high in myxœdema. Moreover, Turner and Steiner found that thyreoid administration produced a sharp drop in serum cholesterol level in every case in their series.

I have myself controlled hyperlipæmia and hypercholesterolæmia with continuous thyreoid administration over a period of almost three years in a patient with hyperlipæmia and eruptive xanthoma secondary to chronic pancreatitis (Flynn and Hall, 1949).

The incidence of atheroma in Iceland is remarkably low (although there the diet is rich in animal fat); but it has been suggested that this may be due to the abundant iodine supply in the food, soil and air of that country.

It is possible that esterases in the blood and arterial wall may be influenced by chemical or endocrinal factors.

Atheroma is also uncommon in China, as are other conditions involving disturbance of lipoid metabolism. However, the Chinese diet for the masses is low in animal fat content.

Suggestions for further lines of research are as follows: (i) The elaboration of a lipoid tolerance test (analogous to a glucose tolerance test) of some type to detect susceptible persons—that is, persons with a disordered lipoid metabolism who are particularly apt to develop atheromatosis lesions. Setala (1948), and Becker, Meyer and Necheles (1949) have already made a start along these lines in their studies of chylomicron curves. Another possible lipoid tolerance test would be the study of serial

TABLE II.

Animal Fats. Average Servings of Some Common Foods.

Grammes of Substance.	Item of Food.	Fat Content. (Grammes.)
	With Fat Content of More than 4·0 Grammes.	
5	Butter	4·0
30	Cheese, American	9·7
30	Cheese, cream	11·0
30	Cream, heavy	10·6
30	Cream, light	6·0
18	Egg yolk	5·1
240	Milk	9·4
5	All oils and fats	5·0
30	Bacon, cooked, crisp	8·1
60	Frankfurt	8·5
90	Halibut	4·8
120	Liver	4·0
90	Mackerel	6·9
90	Meat, lean	12·6
90	Meat, medium fat	16·2
90	Poultry	4·2
90	Salmon, fresh	12·0
90	Salmon, canned	5·7
60	Tuna	7·1
90	White fish	6·0
	With Fat Content of 3·9 to 2·0 Grammes.	
30	Milk, condensed	2·6
30	Milk, evaporated	2·5
90	Bluefish	3·6
30	Salmon, smoked	2·8
30	Sardine	3·3
	With Fat Content of 1·9 to 1·0 Grammes.	
12	Anchovy	1·2
30	Beef, dried	1·9
60	Crab, cooked	1·7
60	Lobster	1·1
90	Oysters	1·2

total serum lipoid levels after the ingestion of a standard fatty meal. (ii) The further investigation of enzyme systems in the arterial walls and of means of influencing them. (iii) The investigation of normal serum cholesterol and lipoid concentration in various countries, and comparison of the diets and the incidence of atheroma in those countries. (iv) The determination, if practicable by some relatively simple means, of the average blood fatty acid level or the average serum lipoid level, and comparison with these of readings from patients with atherosclerosis or from subjects with a disordered lipoid metabolism, who may be candidates for early vascular degeneration. (v) Study of the effects of detergents and pancreatic lipase on the serum lipoids.

THE CONTROL OF ATHEROMA IN SUSCEPTIBLE INDIVIDUALS.

Pending the result of further investigations, it is suggested that an attempt be made to prevent or delay the onset of atheroma by the following measures: (i) Restriction of caloric and fat intake for all overweight subjects, particularly if they have a bad family history with reference to vascular accidents. However, the reduction process should not be too vigorous in relation to these obese persons, as the rapid mobilization of fat from the depots may cause a transport hyperlipæmia, which in turn may lead to intimal deposition of fat particles with the accelerated development of atheroma, or even the precipitation of arterial occlusion. (ii) Restriction of fat intake and substitution of animal fat by vegetable fat in the care of patients who are not overweight but have a particularly bad family history with regard to vascular accidents, especially if they have a raised serum cholesterol level or hyperlipæmia. (iii) To the two classes of subjects mentioned above, the administration of: (*a*) a diet rich in proteins and oxytrophic members of the vitamin *B* complex (nicotinic acid, thiamine, riboflavine), and small

TABLE III.

Cholesterol. Average Servings of Foods of Animal Origin Arranged According to their Content of Cholesterol.[1]

Grammes of Substance.	Item of Food.	Cholesterol Content. (Grammes.)
	With a Cholesterol Content of More than 0·5 Gramme.	
90	Brain, beef	2·124
90	Liver, lamb	0·549
	With a Cholesterol Content of 0·49 to 0·10 Gramme.	
90	Beef, medium fat	0·113
90	Crab	0·131
50	Egg, whole	0·234
18	Egg, yolk	0·360
90	Heart, beef	0·135
90	Kidney	0·369
90	Liver, beef	0·288
90	Liver, calf	0·324
90	Liver, pork	0·378
90	Oysters	0·207
90	Sweetbread	0·252
90	Tripe	0·135
90	Veal, shank	0·126
	With a Cholesterol Content of 0·09 to 0·01 Gramme.	
90	Beef, lean	0·085
15	Butter	0·042
30	Cheese, American	0·048
30	Cheese, Swiss	0·044
30	Cheese, Velveeta	0·048
30	Cheese, Limburger	0·041
30	Cheese, pimento	0·042
90	Chicken, dark	0·045
90	Chicken, light	0·081
90	Codfish	0·045
90	Duck	0·063
90	Lamb	0·063
90	Pork	0·054
90	Salmon	0·054
60	Shrimp	0·090
90	Veal, breast	0·090

[1] Cholesterol is found only in products of animal origin. Foods of vegetable origin contain not cholesterol itself, but other sterols. Sterols contributed by vegetable food need not be considered when the cholesterol content of a diet is being computed, since mammals absorb plant sterols with difficulty or not at all.

amounts of thyreoid hormone; (*b*) lipotropic factors of the vitamin *B* complex (choline, inositol and pyridoxine, to decholesterolize tissue depots); (*c*) adequate amounts of colloidal substances, such as lecithin and albumin, in order to stabilize the plasma cholesterol. (iv) To patients with overt atherosclerosis of the coronary vessels, aorta or cerebral vessels the application of the same dietary precautions.

REPORT OF A CASE.

An example of an obviously susceptible individual is given in the history of a patient examined by me in recent months.

B.C., aged twenty-eight years, consulted me about some small yellow plaques which had appeared on his eyelids about six months previously. I suggested that he should have a serum cholesterol estimation done. The serum

cholesterol level was 630 milligrammes per 100 millilitres. The serum had a faintly milky appearance. The patient was a slightly built young man, with a normal basal metabolic rate and a normal response to the glucose tolerance test. There was, therefore, no obvious cause for the hypercholesterolæmia or hyperlipæmia. However, Thannhauser states that if the serum cholesterol content is more than 300 milligrammes *per centum* and if *xanthoma planum*, no matter how small, is observed, it may be assumed that other organs are involved simultaneously. There was no definite clinical or electrocardiographic evidence of cardio-vascular disease in this man, but his family history was of considerable interest. His father died at forty-eight years from cerebral hæmorrhage; he had also suffered from *diabetes mellitus*. The patient's paternal uncle had died at forty-two years from a coronary occlusion.

Comment.

This man is then obviously a candidate for early vascular degeneration. I consider that it is most important that his diet should be controlled and that every effort should be made by means of diet and the administration of thyreoid, vitamin *B* complex *et cetera* to reduce his hypercholesterolæmia and hyperlipæmia to a normal level.

Other obviously susceptible subjects are people belonging to "cholesterol families", of which many have been reported in the literature. However, these are extreme examples, and I believe that there must be a large percentage of susceptible people in the population who could be saved from an early cardio-vascular demise by appropriate dieting and treatment if they could be detected.

It is important to pay attention to the family history in all cases and to be on the alert for possible stigmata of early vascular degeneration, such as xanthelasma, premature *arcus senilis*, premature greying of the hair and general premature aging in appearance.

Diet Charts.

A sample diet poor in animal fats and cholesterol and containing large amounts of nicotinic acid, riboflavine, thiamine, choline, pyridoxine, lecithin and iodine is attached. It is included as a guide for the dietetic control of atheroma in susceptible subjects. A list of foods rich in animal fats and cholesterol is also attached, as a guide to the foods to be avoided in excess by these subjects.

Suggested Sample of a Menu for a Day.

For a diet poor in animal fats and cholesterol, with large amounts of nicotinic acid, riboflavine, thiamine, choline, pyridoxine, lecithin and iodine, the following is suggested (Table I). The amount of iodine present is indicated by the "+" sign according to the nearest estimation (up to "++++"). Lecithin is present in egg-yolk (11%) and in milk. The quantitative determination of choline and pyridoxine is as yet uncertain, but when appreciable amounts of the vitamin *B* complex are in the diet, choline and pyridoxine are present in sufficient amounts.

Summary.

1. A brief review of modern views on the pathogenesis of atheroma has been given, with particular reference to disordered lipoid metabolism.

2. Suggestions for further clinical and experimental research have been made, some of which are at present under investigation.

3. The opinion is expressed that attempts should be made to control the onset and progress of atheroma in persons who are obviously susceptible on clinical grounds. Methods for doing this have been suggested.

4. Methods for detecting susceptible subjects have been discussed, and the clinical history of a susceptible subject has been given.

5. Diet charts are attached as a guide for the dieting of susceptible individuals.

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References.

Allbutt, C. (1915), "Diseases of the Arteries"; quoted by Boyd, W., *loco citato*.

Becker, G. B., Meyer, J., and Necheles, H. (1949), "Fat Absorption and Atherosclerosis", *Science*, Volume CX, page 529.

Boas, E. P., Parets, A. D., and Adlersberg, D. (1948), "Hereditary Disturbances of Cholesterol Metabolism: A Factor in the Genesis of Atherosclerosis", *American Heart Journal*, Volume XXXV, page 611.

Boyd, W. (1943), "Text Book of Pathology", Fourth Edition, page 394.

Flynn, L., and Hall, G. (1949), "Hyperlipæmia with Secondary Xanthomatosis in Chronic Pancreatitis", THE MEDICAL JOURNAL OF AUSTRALIA, Volume I, page 842.

Gavey, C. J. (1949), "Cardiology of Old Age", *The Lancet*, Volume II, page 725.

Goldblatt, H., Lynch, J., Hanzal, R. F., and Summerville, W. W. (1934), "Studies on Experimental Hypertension. I. Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischæmia", *The Journal of Experimental Medicine*, Volume LIX, page 347.

Gordon, G. (1947), "Mechanism of Lipophage Deposition in Atherosclerosis", *Archives of Pathology*, Volume XLIV, page 247.

Hueper, W. C. (1944), "Arteriosclerosis", *Archives of Pathology*, Volume XXXVIII, pages 162, 245 and 350.

——— (1945) "Arteriosclerosis", *ibidem*, Volume XXXIX, pages 51, 117 and 187.

Leary, T. (1935), "Pathology of Coronary Sclerosis", *American Heart Journal*, Volume X, page 328.

Moreton, J. R. (1948), "Physical State of Lipids and Foreign Substances", *Science*, Volume CVII, page 371.

Mortensen, M. A. (1925), "Is Arteriosclerosis an Hereditary Constitutional Disease?", *The Journal of the American Medical Association*, Volume LXXXV, page 1696.

Muir, R. (1936), "Text Book of Pathology", Fourth Edition, page 297.

Schoenheimer, R. (1949), "The Dynamic State of Body Constituents", Harvard University Monograph in Medicine and Public Health, Number 3, page 23.

Setala, K. (1948), "Preliminary Observations on the Effects of Irradiation upon the Chylomicrons in Human Blood", *Radiology*, Volume L, page 803.

Shivelhood, E. K. (1948), "Myocardial Infarction in Twelve-Year-Old Boy with Diabetes", *American Heart Journal*, Volume XXXV, page 665.

Thannhauser, S. J. (1940), "Lipidoses. Diseases of the Cellular Lipid Metabolism", page 62.

Turner, K. B., and Steiner, A. (1939), "A Long Term Study of the Variations of Serum Cholesterol in Man", *The Journal of Clinical Investigation*, Volume XVIII, page 45.

Wilens, S. L. (1942), "Distribution of Internal Atheromatous Lesions in Arteries of Rabbits on High Cholesterol Diet", *The American Journal of Pathology*, Volume XVIII, pages 63 and 77.

Wright-Smith, R. J. (1936), "Coronary Obstruction", *Royal Melbourne Hospital Clinical Reports*, Volume VII, page 2.

Yater, W. M., Traum, A. H., *et alii* (1948), "Coronary Artery Disease in Men 18 to 39 Years of Age, Report of 866 Cases, 450 with Necropsy Examinations", *American Heart Journal*, Volume XXXVI, page 334.

Reports of Cases.

A GYNÆCOLOGICAL PROBLEM.

By C. J. B. ARMSTRONG,
East Maitland, New South Wales.

IN performing a Manchester or vaginal hysterectomy, I often wondered what was the exact position of the ureters and how great was the danger of their injury. To answer the question I performed the following experiment, and for the benefit of those in a similar dilemma I publish it.

In a suitable subject I passed a ureteral catheter, grasped the cervix with a vulsellum, pushed it into its normal position and took an X-ray picture. Then I pulled the cervix down to the vulva and took another. On comparing

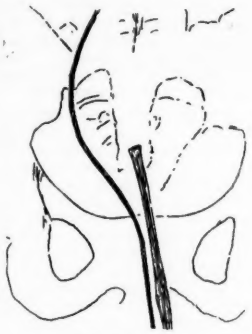

FIGURE I.

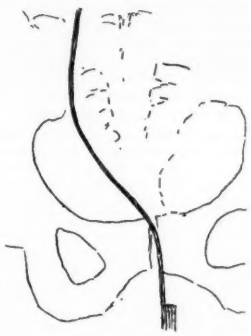

FIGURE II.

the two films one is impressed with the fact that the ureter has not altered its position. Tracings from the two films are published herewith.

The conclusion is that the ureter takes no part in the cystocele and is not especially jeopardized.

Reviews.

THE COMMON INFECTIOUS DISEASES.

DR. STANLEY BANKS, the author of the latest text-book on "The Common Infectious Diseases",[1] is well known to many Australians, who have spent part of their post-graduate studies in England at the picturesque Park Hospital at Hither Green. His book will not disappoint his admirers, and displays to advantage his descriptive powers, his clinical acumen and above all his enthusiasm for his subject. Dr. Banks has always been an enthusiast. He has never been content to accept any form of treatment or concept of a disease as the last word on a subject and many of his original ideas have been adopted into established practice. One might hesitate, however, to accept all the items mentioned in the preface, as originating solely from his teaching.

The many changes that have occurred in this branch of medicine in the last decade have made text-books such as this all the more valuable as books of reference. In addition it is doubly important that the clinical experience obtained by those in charge of fever hospitals during the last thirty years should not be lost to posterity.

A brilliant example of this is seen in the chapter on meningococcal infection. The wealth of clinical detail given on this subject makes one mindful of the descriptive powers of the old masters such as the late Claude Ker. It seems likely that Dr. Banks has written literally the last word on the subject and that later observers will not be able to draw upon such an amount of personal clinical experience.

In general the book attains a high general level of excellence, and it may seem invidious to pick out small items for criticism. While we are grateful for the chapter on diphtheria and especially for Dr. Laurent's contribution on electrocardiography, it is rather disappointing to find such a brief description of laryngeal diphtheria. The management of this disease and other forms of obstructive laryngitis still forms a spectacular part of the work of most fever hospitals. An obvious omission, probably an oversight, is the failure to mention infective mononucleosis in the differential diagnosis of diphtheria. In fairness, however, one must state that in the description of infective mononucleosis this similarity to diphtheria is noted.

In comparison with the older text-books the illustrations of the exanthemata leave much to be desired. It is doubtful whether photographs of rashes in black and white convey any useful help to students. Surely some form of reproduction in colour in modern text-books could be carried out without making the cost prohibitive.

To sum up, one can strongly recommend this book for both pleasant and informative reading and also as a book of reference for students, practitioners and public health workers.

[1] "The Common Infectious Diseases: A Handbook for Students and Postgraduates", by H. Stanley Banks, M.A., M.D. (Glasgow), F.R.C.P. (London), D.P.H. (Cantab.); 1949. London: Edward Arnold and Company. 8¼" × 5¼", pp. 368, with 90 illustrations. Price: 21s.

BUCHANAN'S ANATOMY.

THE eighth edition (1949) of "Buchanan's Manual of Anatomy" shows very little appreciable difference from its predecessor, the seventh edition, which was the first to appear under the editorship of Wood Jones.[1] The format, number of pages and illustrations are the same, though the new edition is some half-inch thicker, probably owing to the use of thicker paper.

For the most part the book is written as a topographical or regional anatomy, though there are several sections of systematic anatomy, including a lengthy one of osteology.

As was stated in the review of the previous edition, there is also an excellent section on the development and growth of the human body. The best of the illustrations, which are all in black and white, are those from the pen of Wood Jones.

There are many references to morphology, but unfortunately there is not nearly enough consideration of the principles of anatomy, or of the relation of structure to function.

For far too long the text and illustrations of text-books of anatomy have been written too much in the manner of street guides and atlases of geography. When the student has to apply his knowledge in the later years of the medical course, he finds to his chagrin, that a very large part of the knowledge that he acquired after long hours of hard work has vanished. Authors of text-books cannot, of course, be expected to take full responsibility for deficiencies in the teaching of anatomy, as after all atlases and guide books are only of value if used correctly, and are not written to be learned by rote. Examiners in anatomy may also be at fault in the method of setting of examination questions. There is much to be said for the concurrent study of anatomy with those parts of surgery with simple underlying pathology, this word being used in the sense of the study of the nature of disease. In this way the student becomes interested in his work, and also learns by practice why anatomy is of importance in the curriculum.

It must be said in conclusion that "Buchanan's Manual of Anatomy" compares very favourably with other books of its type.

[1] "Buchanan's Manual of Anatomy", edited by F. Wood Jones, D.Sc. (London), F.R.S., F.R.C.S. (England), F.R.A.C.S., assisted by E. L. Patterson, M.D., B.Sc. (Manchester), S. Mottershead, M.D., B.Sc. (Manchester), F.R.C.S. (England), T. E. Barlow, M.D. (Manchester), M.R.C.S., L.R.C.P., E. R. Wilde, M.B., Ch.B., B.Sc. (Manchester), F.R.C.S. (England), and Jessie Dobson, M.Sc., B.A. (Manchester); Eighth Edition; 1949. London: Baillière, Tindall and Cox. 8" × 6", pp. 1630, with 847 illustrations. Price: 45s.

MICROCHEMICAL METHODS.

RAPPAPORT'S "Rapid Microchemical Methods for Blood and CSF Examinations" may be regarded as a delayed and enlarged second edition of his *"Mikrochemie des Blutes"*.[2] This appeared in 1937 while the author was working in the *Institut für allgemeine und experimentelle Pathologie*, of Vienna. Political events forced the author to leave Austria before the second German edition, which had been prepared, could appear. The present volume has been prepared while the author was working in Israel.

Apart from the chapter on the analysis of blood gases, which deals exclusively with the methods of Van Slyke and his school, methods developed in European laboratories are usually described. This means in effect that a smaller

[2] "Rapid Microchemical Methods for Blood and CSF Examinations", by F. Rappaport, Ph.D., with a foreword by F. Silberstein, M.D.; 1949. New York: Grune and Stratton, Incorporated. 8¼" × 5¼", pp. 428, with 72 illustrations. Price: $8.75.

proportion of colorimetric methods is employed. No biochemical work, however, can escape being heavily indebted to colorimetric methods. The author's choice of methods, he points out, has been dictated in part by economic considerations. Methods requiring costly photometric apparatus have not been practicable with the facilities at his disposal.

The material considered may be placed in three main groups: determinations of general and physical properties of blood, determinations of ionic constituents, and determinations of non-ionic constituents. In connexion with some of the functional tests it has, of course, been impossible to exclude certain analyses of urine despite the limitation implied by the title of the book. It is a little surprising to find determinations of prothrombin treated in the chapter on vitamins. The use of these determinations is by no means restricted to the control of vitamin *K* therapy.

The directions for the various methods are concisely and clearly given, with frequent use of diagrams. Several of the methods have been developed by the author. An appendix contains instructions for the use of certain types of volumetric apparatus, the preparation of solutions, and the use of some types of colorimeter.

References are given at the end of each chapter to the original sources of the methods described. The book is very well produced, and has a comprehensive index.

OPERATIONS OF GENERAL SURGERY.

THE appearance of a second and somewhat expanded edition of "Operations of General Surgery" by Professor Thomas G. Orr, of the University of Kansas, makes a welcome addition to the number of really useful books.[1] It covers the great majority of standard operations in all branches of surgery, and includes the regular procedures of all the specialties. Where necessary, a brief outline of the relevant anatomy is given, as well as the indications for operation. The common and more important dangers are stressed together with the appropriate precautionary and preventive measures.

The text is profusely illustrated with some 1700 step-by-step illustrations, and in so far as diagrams can aid the operating surgeon, these give a clear indication of the principles involved.

In regard to the more involved modern procedures such as pancreatico-duodenectomy and portal-systemic anastomoses, only the barest outline is given and much more information would be required before an initial attempt at such an operation was made. Considerations of space naturally impose the same limitations on the descriptions of intricate operations in the specialties. However, areas of more common major surgical intervention, such as thyreoid, breast, stomach and hernia, are more fully detailed and give clear and accurate information sufficient to guide those not fully experienced in the regions concerned.

The majority of techniques described are those with which we are familiar in this country, but in addition there are the stimulating variations of modern American practice.

For a surgeon faced with an unfamiliar problem, for the practitioner who wishes to enlarge his surgical repertoire, or for the post-graduate student this volume will be of much assistance.

HEARING TESTS AND HEARING INSTRUMENTS.

WHILE it is undoubtedly true that the otologist is able with very fair accuracy to determine the nature of deafness with the assistance of such simple devices as tuning forks, and the measured voice or whisper, together with his clinical observations, nevertheless the compilation of a book such as "Hearing Tests and Hearing Instruments" by L. A. Watson and T. Tolan will be welcomed by all who seek for scientific accuracy or would strive to know "why".[2] To try to discover the meaning of defective hearing, or to be able to interpret otic histopathology correctly, calls for more precise estimation of perceptive capacity than was possible with the crude methods of but recent years. To fit a hearing aid correctly the deficiency must first be closely calculated. To assess cochlear function and determine suitability for a fenestration operation, and later to record the gain achieved, both for pure tone perception and in the matter of efficiency of comprehension of spoken words, calls for the use of finely calibrated audiometers and the application of scientifically developed word tests. The interpretation of the results in terms of percentage gained and of subsequent social adequacy has to be understood.

In this excellent book the authors contrive to put together, in as simple a fashion as a scientific subject will permit, the knowledge of audiometry which has been developed especially in the past twenty years. The instruments themselves are described in practical fashion, and much of the newer studies of pure tone audiometry together with speech and social adequacy hearing estimation is outlined. To cover a subject so technical in a comparatively small book and without introductory theory the authors obviously assume in the reader some knowledge of the physics of sound and of acoustics, as well as an understanding of practical otology. The book is thus for the use of otologists and audiometrists and will serve each equally well as a summary of modern development in audiology. For those who would proceed to academic or research work in audiology this text should provide an excellent introduction. It is definitely not a book for the beginner, neither will all of its technical details be always clear to the otologist who has forgotten his physics or who has failed to keep moderately well informed of the trends in practical audiology. To those who have a broad understanding of the subject and wish for a compendium from which to refresh the memory, or to clarify a problem, this work should prove most valuable. Its worth is reinforced further by a complete bibliography. This is a work which the otologist has for some time hoped for, and the authors will surely have the gratitude of all who turn their interests to the problems of hearing and of deafness and the methods and instruments available for its alleviation.

ELECTROCARDIOGRAPHY.

IN "Electrocardiography: Fundamentals and Clinical Application", Louis Wolff has not produced merely another detailed description of normal and abnormal electrocardiograms. He assumes that the reader is conversant with the simpler sections of electrocardiography, for example, those of the arrhythmias, heart block *et cetera*, but for one who has studied the subject, the book is both interesting and instructive. It is divided into two parts. In the first the author attempts to engender an understanding of electrocardiograms by correlating sufficient relevant fundamental facts of the physics and physiology of the heart. In doing so, he does not go into unnecessary detail, but merely enough to form a frame-work on which to build the pattern likely to be produced by certain cardiac conditions. The second part consists of the application of the rules and guiding principles, to the interpretation of electrocardiograms in conditions in which important information may be derived for the assistance of the clinician. The author puts the reader's understanding of the first part to the test by advising him to picture for himself the probable outline of the electrocardiogram under certain circumstances, after which he exhibits the illustration and its explanation. He gives due consideration to hypertrophy of the ventricles and left and right bundle branch lesions. One might question the stress that he places on the left ventricular complex which is sometimes recorded in *V*1 in the presence of right ventricular hypertrophy. Surely the emphasis should be placed more on the rotation than the hypertrophy? This, of course, is a very minor matter, and not one of much clinical importance. The author considers in detail the changes produced by pericarditis and by pulmonary infarction, but he pays most attention, however, to the effects of coronary occlusion. In reading this section, one is still further impressed by the help to be obtained from multiple unipolar leads, for the author has shown how they may be used to the best diagnostic advantage. In addition, attention is focused on the alterations produced in the picture by additional infarcts,

[1] "Operations of General Surgery", by Thomas G. Orr, M.D.; Second Edition; 1949. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10¼" × 7¾", pp. 908, with 1700 illustrations. Price: £6 8s. 3d.

[2] "Hearing Tests and Hearing Instruments", by Leland A. Watson and Thomas Tolan, M.D.; 1949. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson. 9" × 6¼", pp. 612, with 239 illustrations. Price: £3 15s. 3d.

[1] "Electrocardiography: Fundamentals and Clinical Applications", by Louis Wolff, M.D.; 1950. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 9¼" × 6¼", pp. 192, with 110 illustrations. Price: 42s. 9d.

pericarditis *et cetera*. His final chapter, not surprisingly, considers the Wolff-Parkinson syndrome.

The author has compiled a useful and stimulating little book which is an efficient aid to accurate interpretation, but at the same time he stresses the importance of keeping within bounds when making interpretations, and of not reading too much into tracings. The author has not perhaps presented a great deal that is new, but he has made the details of the picture stand out in sharp relief. This book can be recommended with confidence to the cardiologist.

ALLERGY.

THE author of "Allergy: What It Is and What to Do About It", one Harry Swartz, has stated in his introduction that the intention of his book is to clarify misconceptions.[1] The coverlet declares his intention to make the mystery of allergy understandable to the layman and to tell of the latest developments. The effort is praiseworthy, but not satisfactory. The book is neither detailed enough for use by medical men nor simple enough to be understood by the layman. Dr. Swartz covers an immense amount of ground in 200 pages, dealing with the early history, the causes, the symptoms and the treatment. Much valuable and accurate information is given which is a summary of present knowledge according to the author's beliefs, but with all of which not everyone will agree, though all may receive some profit from it. The layman must be indeed confused when he meets a paragraph beginning: "Often what seems a definite qualitative difference is simply a quantitative one. Life rose from non-living matter by a process of rearrangement of dynamic energy pattern. The fundamental difference between living and non-living matter is in energy arrangement. In the living, energy is free floating, momentarily utilizable, volatile, reactive. Although the energy in non-living matter is for the most part dormant, chemical reactions show that it can be called into great activity under certain circumstances. . . ."

The thoughtful provision of a glossary of medical terms at the end of the book will, one fears, do little to clarify the present position in regard to allergy in the mind of the layman—at least, the Australian layman. But, if he does read through the book, he cannot fail to be impressed with the magnitude and scope of the subject and the extreme difficulty with which satisfactory treatment is encompassed.

RATIONAL MEDICINE.

"RATIONAL MEDICINE", by J. W. Todd, is an interesting book originally written while the author was serving in the army abroad.[2] It is a work which deals largely with perspective and orientation in medical matters, and the fact that it was favourably received by the late Professor Ryle, who, incidentally, suggested its title, is in itself a strong recommendation. After an initial chapter on the need for diagnosis, in which he stresses the fact, so often overlooked, that diagnosis is not an end in itself, the author gives a critical appraisal of various signs and symptoms and discusses the value of certain accepted forms of treatment. He then deals at length and in a revealing way with that aspect of medicine which is now designated by the adjective psychosomatic. This section is the highlight of the book and deserves to be read by all who deal with patients, but especially by those who tend to view them within the restricted horizons of their own particular speciality.

The theme of the book is the necessity for regarding the patient not as a conglomeration of organs, but as an integrated human being—a real person. Dr. Todd accuses many of his colleagues of a form of mental dichotomy, keeping in a separate compartment of their brains all the knowledge of men acquired in their ordinary lives and applying, when dealing with patients, only that knowledge gained professionally. The imaginative history of a neurotic female from conception to the grave is a particularly good piece of writing and is used to indicate the enormous number of incorrect organic diagnoses with which such an individual can be labelled.

The chapter on constipation "debunks" the lucrative myth of "inner cleanliness" and recalls the excellent article in this journal some 15 years ago by Dr. Lethbridge on "The Pandemic of Aperientitis".

The points on which one would differ from the author are of minor importance (except his statement on page 95 that "negative radiography" definitely excludes pulmonary tuberculosis). In view of the prevalent habit of young graduates to regard patients as "cases", the book can be recommended to them as a means of giving the correct approach to the practice of medicine in addition to supplementing their experience in the fertile psychosomatic field.

THE TUBERCULOUS PROCESS.

THE subtitle of Dr. Alfred Leitch's little book on "The Tuberculous Process" is "A Conception and a Therapy".[1] The conception, as he explains in the first paragraph, is that the tubercle bacillus cannot thrive and bring about its characteristic action in an animal body which has not been subjected to some malign influence. In attempting to substantiate this notion he does not "seek out the truth by way of experiment", but proceeds by a chain of reasoning from a series of postulates. He postulates that the tubercle bacillus is a saprophyte which gives rise to methyl radicles when grown in decaying animal tissue; that it there secretes an enzyme or enzymes which enable it to obtain its nourishment; and that it cannot grow in normal tissue owing to the presence of an anti-enzyme, formaldehyde, which is stated to be an intermediate substance in normal carbohydrate catabolism. In the final chapter he proposes a "rational therapy" of tuberculosis by means of the administration of a solution of hexamine containing a little formaldehyde, together with an adjuvant mixture containing benzoic acid, powdered camphor and aniseed oil. The book concludes with case reports of sixteen patients whose health improved after this medication, but the bacteriological or radiological evidence that they were in fact suffering from tuberculosis is presented in only one.

DIAGNOSIS AND TREATMENT OF TROPICAL DISEASES.

WITHIN the 147 pages of his "Epitome of Laboratory Diagnosis and Treatment of Tropical Diseases" Dr. Horace M. Shelley has succeeded in his object of supplying the tropical practitioner with simple details of these two important aspects of the subject.[2]

The diagnostic sections include details of staining methods and simple laboratory tests, which are mainly within the competence of doctors without specialized training in clinical pathology. The inclusion of a brief account of a serological method for the diagnosis of syphilis, however, is not so useful, for in such work some training and practice are needed if reliable results are to be assured.

The summaries of treatment generally are satisfactorily presented. In presenting the treatment of malaria, however, the author offers little guidance to inexperienced readers. Methods are listed (including the use of tebetren, quiniostovarsol and methylene blue), but apart from a note that "Atebrin" is considered the best preparation for general use until the value of "Paludrine" is proven, the choice of these rests largely with the reader. Chloroquine and pentaquine are not mentioned in this section, though the former is listed as "Aralen" in a useful "compendium of drugs in use in tropical medicine" which appears later. As the treatment of infants and children frequently offers difficulty to practitioners who see only occasional cases of malaria, it could with advantage be dealt with more fully, and the problem of relapses in benign tertian malaria should be more adequately considered. The section on amœbic dysentery gives a useful discussion of the commonly used drugs, but omits consideration of effective courses of treatment.

[1] "Allergy: What It Is and What to Do About It", by Harry Swartz, M.D.; 1950. London: Victor Gollancz, Limited. 7¾" x 5¼", pp. 228. Price: 9s. 6d.

[2] "Rational Medicine", by John W. Todd, M.D. (London), M.R.C.P. (London); 1949. Bristol: John Wright and Sons, Limited. London: Simpkin Marshall (1941), Limited. 8¼" x 5⅝", pp. 392. Price: 25s.

[1] "The Tuberculous Process: A Conception and a Therapy", by Alfred Leitch, M.B., Ch.B. (Edinburgh); 1949. Bristol: John Wright and Sons, Limited. London: Simpkin Marshall, Limited. 7½" x 5", pp. 188. Price: 12s. 6d.

[2] "An Epitome of the Laboratory Diagnosis and Treatment of Tropical Diseases", by Horace M. Shelley, F.R.F.P.S., M.R.C.P. (London), D.T.M. and H. (England); Second Edition; 1949. London: Staples Press, Limited. New York: Staples Press, Incorporated. 8½" x 5½", pp. 150, with a few illustrations. Price: 10s. 6d.

In the treatment of helminth infestation the use of tetrachlorethylene is disregarded, and mention of the recent specific therapy for filaria omitted. The deficiencies that exist, however, are mainly the result of condensation.

This book does not replace the more detailed text-books on tropical practice, but provides a useful reference work in a short form.

HORMONES AND THEIR USE IN GENERAL PRACTICE.

W. N. KEMP has attempted the task of indicating the therapeutic applications of the various hormonal preparations now available to the medical profession, and in addition he has endeavoured "to clarify the multitude of trade names that have been applied to the various hormones by different commercial organisations". He presents the subject on a series of cyclostyled sheets bound with a coiled wire.[1] After giving a short historical review of endocrinology, he describes the various endocrine disorders and their treatment. In the last chapter the differential diagnosis of the endocrinopathies is summarized and a table of normal values of the chemical contents of the blood is appended. The description of the clinical features of the ductless gland disorders is well done, but insufficient details of treatment are given. The book is marred by numerous typographical errors and the absence of illustrations is a disadvantage. To the Australian reader the omission of the names of a number of the well-known British preparations is a serious drawback.

While every medical practitioner must feel sympathetically inclined to an author who essays such a formidable task as Kemp has done, it is our opinion that the book does not give the information which one hopes to find in it.

APPLIED DIETETICS.

THE third edition of "Stern's Applied Dietetics" was being prepared by Frances Stern prior to her death in 1947, and it now appears revised by Helen Rosenthal, Pearl C. Baker and Wilma A. McVey, who were the author's associates at the food clinic of the Boston Dispensary.[2] Modern dietetics is as much a science as any other branch of medicine, and this book is a comprehensive treatise on the subject. The work is divided into four sections. Part one is devoted to introductory chapters on such subjects as the daily food requirements of the body, the construction of normal and therapeutic diets and the education of the patient in regard to both normal and therapeutic diets. Part two contains some sixty-two tables, which are invaluable, for they enable the contents of any dietary constituent to be assessed exactly, and so it is only a matter of turning to the appropriate table to know, for example, how much copper is in a certain foodstuff, or how much fat is contained in an average serving of various meats. Other important data set out in tabular form are the various food exchanges, enabling one item to be substituted for another of equal food value while the same proportion of the essential constituents is kept. This exchange is important both from a monetary viewpoint with regard to the patient's purse and also from the angle of seasonal variations when some foods become scarce. Part three consists of outlines for diets, both normal and therapeutic. Naturally diabetic diets are featured prominently and so, too, are diets for sufferers from nephritis, heart disease and all the various gastro-intestinal upsets from peptic ulcers to constipation. Vitamin deficiencies, too, are fully discussed and the important part played by food in pregnancy and lactation is stressed. Part four is made up of examples of typical diets and menus, and from these and the various tables all types of diets can be readily constructed with almost molecular exactitude. Dietitians and physicians alike will benefit from the wealth of detail which makes this book most valuable.

[1] "The Value of Hormones in General Practice", by W. N. Kemp, M.D.; 1949. Minneapolis: Burgess Publishing Company. 11" × 8", pp. 115. Price: $3.00.

[2] "Stern's Applied Dietetics: The Planning and Teaching of Normal and Therapeutic Diets", revised by Helen Rosenthal, B.S., Pearl C. Baker, B.S., and Wilma A. McVey, M.D.; Third Edition; 1949. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 10" × 7", pp. 318. Price: 53s. 9d.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Aids to Materia Medica", by George H. Newns, M.D. (London), M.R.C.P. (London); Fourth Edition; 1950. London: Baillière, Tindall and Cox. 6¼" × 4", pp. 212. Price: 5s. net.

One of the "Students' Aids Series". Intended for students reading for examinations. In this edition have been included the drugs contained in the British Pharmacopœia, 1948.

"Medical Jurisprudence and Toxicology", by John Glaister, J.P., D.Sc., M.D., F.R.S.E.; Ninth Edition; 1950. Edinburgh: E. and S. Livingstone, Limited. 8½" × 5½", pp. 768, with many illustrations, some of them coloured. Price: 35s.

The eighth edition was published in 1945 and revised in 1947.

"Industrial Health: An Introduction for Students", by R. Passmore, M.A., D.M., F.R.S.E., and Catherine N. Swanston, M.R.C.S., L.R.C.P., D.P.H., D.I.H., with a foreword by Professor F. A. E. Crew, F.R.S.; 1950. Edinburgh: E and S. Livingstone, Limited. 7" × 5", pp. 118. Price: 4s. 6d.

An attempt to make "a brief statement of the rules of industrial hygiene" by a lecturer in physiology and a lecturer in industrial health.

"Notes on Communicable Diseases of Laboratory Animals", by H. J. Parish, M.D., F.R.C.P.E., D.P.H.; 1950. Edinburgh: E. and S. Livingstone, Limited. 7" × 5", pp. 76. Price: 3s.

Sections are devoted to the several animals and the diseases of each are described in the telegraphic style.

"Clinical Examination of Patients with Notes on Laboratory Diagnosis", by J. Forbes, M.D., M.R.C.P., and W. N. Mann, M.D., F.R.C.P.; 1950. London: Edward Arnold and Company. 8½" × 5½", pp. 343, with many illustrations. Price: 18s. net.

Intended as a guide to the student during his introduction to clinical medicine.

"The Hinge Graft or Ginglymus Implant", by Arnold K. Henry, M.B. (Dublin), M.Ch. (Hon. Cairo), F.R.C.S.I.; 1950. Edinburgh: E. and S. Livingstone, Limited. 9½" × 7", pp. 72, with 47 illustrations. Price: 15s.

A practical treatise describing and illustrating the hinge graft in various conditions.

"Non-Gonococcal Urethritis: Including the Genital Manifestations of Local and Systemic Diseases and Infestations of the Urinary Tract with Protozoa, Metazoa and Fungi", by A. H. Harkness, M.R.C.S., L.R.C.P.; 1950. Edinburgh: E. and S. Livingstone, Limited. 9¾" × 7", pp. 434, with 167 illustrations, some of them coloured. Price: 52s. 6d.

The author regards gonorrhœa as a dying disease and discusses non-gonococcal urethritis under the headings of the causative organisms.

"Introduction to Neuropathology", by Samuel Pendleton Hicks, M.D., and Shields Warren, M.D.; 1950. New York, Toronto and London: McGraw-Hill Book Company, Incorporated. 9¾" × 7", pp. 508, with many illustrations. Price: $10.00.

Designed to introduce the fundamentals of neuropathology to medical students and trainees in neurology and pathology, and to stimulate an interest in the subject among general pathologists.

"Developments in Diphtheria Prophylaxis", by Lewis B. Holt, M.Sc.; 1950. London: William Heinemann (Medical Books), Limited. 9" × 7½", pp. 198, with illustrations. Price: 42s.

Covers work on the subject during the last ten years.

"Textbook of Gynæcology", by J. H. Peel, M.A., B.M., B.Ch. (Oxon.), F.R.C.S., F.R.C.O.G.; Third Edition; 1950. London: William Heinemann (Medical Books), Limited. 8½" × 5¾", pp. 494, with 219 illustrations. Price: 24s.

Intended for undergraduate students.

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RETROLENTAL FIBROPLASIA AND PREMATURITY.

THE condition now generally known as retrolental fibroplasia was first observed by T. L. Terry in 1941. His definition of the term, as quoted by A. C. Krause,[1] is as follows:

> The development of embryonic connective tissue in the meshwork of the persistent hyaloid artery system behind the crystalline lens as a result of improper development of the inner eye, usually developing 3 to 5 months after birth in the extremely premature infant, is a disease entity which I call "retrolental fibroplasia".

The typical features of the disease are, according to Terry,[2] an opaque vascularized membrane behind the lens, microphthalmia, shallow anterior chambers, fœtal-blue colour of the iris, thin ciliary processes in front of the opaque tissue, searching nystagmus, apparent photophobia, persistent hyaloid artery and often retinal separation. A good deal of confusion has occurred in the differentiation of this condition from others with similar features but with allegedly essential differences in nature. In the paper already quoted, Krause reports 18 cases of a similar condition with additional features that he terms "congenital encephalo-ophthalmic dysplasia". Algernon B. Reese[3] has drawn a careful distinction between retrolental fibroplasia and what he calls "persistence and hyperplasia of the primary vitreous". There is, however, by no means general agreement about these other conditions described, nor indeed about the suitability of the term retrolental fibroplasia, and it may be recalled that F. B. Walsh is reported to have said, when speaking at the Australasian Medical Congress (British Medical Association) in Perth in 1948,[4] that if infants were premature with small eyes, and if the condition was bilateral, they should in the present state of knowledge be included in the retrolental fibroplasia group. The question is to some extent academic, but is of interest and will no doubt be settled in time; meanwhile there are more urgent practical aspects. Terry calculated that in the United States over 10% of the infants born prematurely, weighing three pounds or less at birth, could be expected to be blind from retrolental fibroplasia. Reese, from a consideration of available data in the United States, estimates that one-third of all cases of blindness in pre-school children now are due to retrolental fibroplasia. The condition is being increasingly observed in England. From this it is clearly important that an understanding be obtained of the ætiology and that effective prophylaxis and/or treatment be devised if possible. In a recent clinical study of 238 cases of retrolental fibroplasia (Terry's original 117 and an additional 121), M. J. King,[1] who has had much experience in this field and has carried on Terry's work, states quite bluntly that the cause of the condition is still unknown. Prematurity and small weight at birth are predisposing factors in a large majority of cases. The incidence appears to be greater in certain localities than in others, according to King, though no explanation for this is apparent. The increased incidence is not accounted for by failure to make the diagnosis in the past or, primarily at least, by a significant increase in the survival rate of premature infants. Whether the condition is congenital or not is still disputed. The fact that its appearance is noted some time after birth has aroused discussion and conjecture. W. C. Owens and E. U. Owens[2] examined 214 children whose birth weight was four and a half pounds or less. None had retrolental fibroplasia at birth, but of 111 followed for six months or more, five developed the condition. Owens and Owens also followed nine premature children who developed retrolental fibroplasia between two and five months of age. All visible remains of the hyaloid system had disappeared before the onset of the disease. The fundus picture was initially normal and was then replaced by an angiomatous dilatation of the retinal vessels, followed by massive retinal exudation, retinal detachment and the formation of a retrolental membrane. Owens and Owens feel, from their observations, that retrolental fibroplasia occurring in premature infants is not due to an arrest in growth or aberration of some embryonic or fœtal structure; it is not related to persistence of the hyaloid vessels; it is not a congenital condition. Various possible ætiological factors mostly operating in the period immediately after birth have been considered. V. E. Kinsey and L. Zacharias[3] found a higher incidence of the condition among male infants, among the offspring of *multiparæ* and among those who remained in the nursery or incubator or received oxygen treatment for long periods. Further investigation revealed that the incidence apparently increased with the total amount of water-miscible vitamins and iron given. The significance of these findings does not seem to have been further elucidated. Owens and Owens[4] have made some striking observations which suggest that deficiency of vitamin *E* intake may be of ætiological importance. This possibility, originally adduced from observation of diets, appears to have been supported by subsequent controlled experiments with the administration of supplements of vitamin *E* to infants of birth weight

[1] *Archives of Ophthalmology*, October, 1946.
[2] *The Journal of the American Medical Association*, June 23, 1945.
[3] *Archives of Ophthalmology*, May, 1949.
[4] THE MEDICAL JOURNAL OF AUSTRALIA, October 9, 1948.

[1] *Archives of Ophthalmology*, April, 1950.
[2] *Transactions of the Ophthalmological Society of Australia*, Volume VIII, 1948.
[3] *The Journal of the American Medical Association*, February 26, 1949.
[4] *American Journal of Ophthalmology*, December, 1949.

less than three pounds. It is stated that vitamin *E* supplements are of no value if not started at least before the baby is six weeks of age, since by that time irreversible retinal changes have occurred. Confirmation and elaboration of this work will be awaited with much interest. Another possible ætiological factor that has been suggested is the premature exposure of the infant's eyes to light, but a careful investigation carried out by W. R. Hepner, A. C. Krause and M. E. Davis[1] has failed to provide any support for the suggestion. One possibly significant feature of retrolental fibroplasia is its observed association with multiple angiomata scattered over the body; Reese, in the paper already cited, mentions an incidence of 25% of hæmangioma in children with retrolental fibroplasia, though in a report[2] of the paper that he presented, with F. Blodi, at the International Congress of Ophthalmology in London in July, 1950, the incidence quoted is only 18%; this is nearer the 17% quoted by King, who points out that it is not much greater than the 15% incidence found by Kinsey and Zacharias in premature infants who did not have retrolental fibroplasia. However this may be, B. Klien[3] has reported findings of angioblastic overgrowth of the primary vitreous which may be related to the development of retrolental fibroplasia, and Reese and Blodi with their paper showed slides demonstrating the presence of angioblastic tissue in the retina of babies affected with retrolental fibroplasia during the active stage, which was stated to last about ten weeks. Reese has suggested the possibility that a modified form of X-ray therapy may be helpful as a preventive measure if the hæmangiomatous factor proves to be significant, but the matter needs a good deal of further investigation. Growing concern at the increasing incidence of the disease demands that every reasonable clue be followed. So far the investigation of ante-natal factors has not been productive, according to H. Speert *et alii*,[4] but one cannot help feeling that, in the midst of a great many conflicting facts and unproven theories relating to ætiology, none of which yet offers a practical line of prevention or treatment, Speert *et alii* offer a rather obvious suggestion that should be heeded, namely, that efforts at reducing the incidence of the disease must be primarily in the direction of prevention of premature birth. The one clear point about the disease is its association with prematurity and low birth weight; our inability yet to interpret the significance of this fact does not make the fact and its overcoming any less important.

Current Comment.

DIABETIC RETINITIS.

A GOOD DEAL has appeared from time to time concerning diabetic retinitis, particularly with regard to its prevention. Some years ago various fractions of the accessory food factors came into prominence in the treatment of this and other vascular disorders, and rutin was tried—in the opinion of some workers, with success—in the control of diabetic retinitis. Another study has been published by Robert H. Barnes on this subject.[1] Rutin has been used to decrease the fragility and permeability of capillaries, and in both diabetic and hypertensive retinopathies it has been thought to have some value, though this is still an open question. Barnes quotes a number of recent authorities who have attempted to assess its effect in diabetics, but their results appear to be little more than a clinical impression. The occurrence of retinal hæmorrhage has also been recorded while the patient was being treated with rutin, although this finding really means little, since it cannot be expected that severe and probably irreversible lesions can be affected by any special treatment. Barnes used a technique for estimating capillary fragility in which pressure from a sphygmomanometer cuff was applied for four minutes, not exceeding 80 millimetres of mercury. The petechiæ produced on the arm were counted in a circle of six centimetres with the aid of a hand lens. A series of 220 patients was studied, and they were divided into categories according to whether they had hypertension or not, and into groups according to the presence or absence of retinitis and of increased capillary fragility. As might be expected, some patients were encountered who had retinitis, but whose capillary system showed no increase of fragility. However, in 80% of those who had retinitis the capillary vessels were unduly fragile. Also, 68 out of 140 patients had weak capillaries but no signs of retinitis. These results confirm the usual findings that diabetes *per se* is associated with increased capillary fragility. In this series, also, hypertension had a definite influence, for it was associated with retinitis and fragile capillaries twice as often as with the absence of these abnormalities. The influence of age was also studied, but this was found to be less significant than the duration of the diabetes. The importance of the observation that juvenile diabetics of long standing were relatively prone to this complication will be duly noted. Barnes presents evidence, as others have done, of the significance of both hypertension and the duration of the diabetes as factors in the production of retinitis. He remarks that poor control of diabetes may lead to early appearance of retinitis. In assessing the value of rutin in the treatment of these patients, he found that this substance had little effect either on the retinitis or on the capillary fragility. He used some patients as controls, but even those who had no evidence of retinitis, but whose capillaries were fragile, showed no change in the blood vessels even after a long course of rutin. Most of the patients were treated for long periods; the shortest was six weeks, but others took rutin for thirty-three months. Large doses, up to 300 milligrammes a day, had no apparent result. In cases of long duration, progress of the retinal lesions was sometimes observed even while the patient was under treatment. Barnes suggests that, though the results of this clinical research are negative, it might be worth while to begin treatment very early, and to observe the course of such a series, checking the findings with regular retinoscopy and estimations of the capillary fragility. He concludes that the place of rutin has not been established in the treatment of diabetic retinitis. One valuable lesson from such work is perhaps obvious, that the best preventive measures for lessening the risk of vascular complications are early diagnosis of diabetes and the prompt institution of treatment, with regular follow-up of the patient. Another interesting example of this principle may be seen in the peripheral neuropathy which has been described as occurring in over 90% of all diabetics. This, of course, has no connexion with retinitis, but, being another metabolic disturbance associated with diabetes, it helps to point the moral. W. S. Collens, A. M. Rabiner, J. D. Zilinsky, L. C. Boas and J. J. Greenwald have recently recorded the results of treating the peripheral neuritic states which they have found so constantly on careful search.[1] Vibration sense was impaired in most of their patients, and in some instances this condition was followed by atrophic lesions in certain muscles, particularly the small muscles of the hands and feet. They regard these lesions as due to disturbance of the vitamin *B* metabolism, and claim that amelioration followed the administration of massive doses of the *B* complex. It would seem logical to assume here also that control of the disease is of first importance

[1] *Pediatrics*, June, 1949.
[2] *British Medical Journal*, August 5, 1950.
[3] *Archives of Ophthalmology*, May, 1949.
[4] *American Journal of Obstetrics and Gynnecology*, February, 1950.
[5] *The American Journal of the Medical Sciences*, April, 1950.

[1] *The American Journal of the Medical Sciences*, May, 1950.

in the prevention of its complications, or at least in minimizing their effects. This would, of course, in no way discourage the attempts to discover specific agents of value in specific metabolic deficiencies liable to occur in a disease of such nutritional importance.

ARTERIOGRAPHY AND BONE TUMOURS.

RADIOGRAPHY of arteries, having appropriated to itself the name of arteriography against several apparently unsuccessful competitors, has made considerable advances as a diagnostic aid in recent years. Its commoner uses are well known, but Reynaldo dos Santos[1] reports an application of the procedure that not only is ingenious, but also has useful possibilities. He explains that the purpose in his work with arteriography has been to determine not only the anatomical distribution of blood vessels, but also the functional circulation of diseased tissues. Simple arteriography gives a picture of the vascular pattern, for example, of a limb, down to the smallest branches at any given moment a few seconds after commencement of injection of the opaque solution; but if a series of films is taken at intervals of one, two and three seconds, it is possible, dos Santos states, not only to assess the morphological appearances, but also to examine the circulation from a dynamic point of view. These ideas have been especially applied to tumours of soft tissue and bone, and dos Santos and those working with him have gained experience in the arteriographic characteristics of bone tumours and learned to recognize significant features in their differential diagnosis from osteomyelitis. Amongst other possibilities the technique may be used to assess the response of malignant bone tumours to treatment by irradiation. Illustrating the paper is a series of arteriograms of considerable interest; they show the appearance in the normal as well as in various abnormal states. Dos Santos states that in malignant bone tumours, serial arteriograms show irregular formation of new vessels of uniform diameter, "blood pools" and increased rapidity of flow from the arterial to the venous systems. In osteoclastomata there is new vessel formation and an appearance of "blood pools", but less rapid filling of the veins. In simple tumours there is no new formation of vessels, and the tumour itself is often relatively avascular. In osteomyelitis there is no new formation of vessels, but only dilatation of existing vessels; the vessels retain their orderly and regular arrangement of successive branches of gradually decreasing diameter. These appearances are considered to be of value in differential diagnosis and also in the assessment of the degree of malignancy of a tumour, as well as in the observation of the response of such tumours to irradiation. The idea appears to have considerable practical possibilities.

THE CONTROL OF CARDIAC FIBRILLATION.

CARDIAC FIBRILLATION usually implies auricular fibrillation, as this condition is of frequent clinical occurrence, and usually, except in association with cardiac failure, need not always of itself cause great anxiety. Ventricular fibrillation may occur, of course, as a terminal event, or may be recognized as part of some cardiac accident or disability, usually of grave nature. Of recent years acute cardiac arrhythmias have been recognized as an important complication of the use of certain anæsthetic agents, such as cyclopropane, or of operations on the thoracic organs. As a number of drugs have now been employed to cut short episodes of fibrillation, and quinidine in particular has now stood the test of time, it is of interest to inquire if there are better alternatives. Joseph R. DiPalma and John E. Schultz have produced a comprehensive review of the antifibrillatory drugs with a bibliography covering the field.[1] It is perhaps surprising to read that, though quinidine has been in use nearly thirty years, and though some of its properties are regarded as accepted facts, not even the several thousand papers which have been written about it have removed confusion in some respects. The authors briefly traverse the facts and theories concerning auricular fibrillation, and point out that recent cinematographic work has supported Lewis's concept of circus movement, though they remark that as a working basis the factors to be considered are the refractory period, the rate of conduction and the length of the path. The quality of irritability of heart muscle has been a source of confusion, for it can be judged only by its results, and means little unless measured in terms of an area of local block. Similarly, the refractory period in auricular fibrillation is important only in so far as the relative refractory period is lengthened by a drug like quinidine. However, it is not possible here to review questions of physiology in detail, since we are more concerned with the nature, effects and mode of action of drugs which are safe to employ when the clinical indications are satisfied. The ideal drug does not yet exist, but the chances of success are greater when these indications are clearly understood. One of the difficulties in investigating the pharmacological action of these drugs is that the hearts of test animals vary greatly in their susceptibility to the initiation and termination of fibrillation according to species. In the human subject fibrillation is a capricious and episodic event. This is best seen in the paroxysmal varieties, which may begin through some obscure stimulus, and may end spontaneously, thus tempting the physician to ascribe this happy result to the treatment employed. It is best, of course, to exclude from our consideration fibrillation observed as an accompaniment of congestive failure, for example, in mitral disease.

The most commonly employed drugs have been the cinchona alkaloids; among these quinidine is preeminent. The great stimulation of malarial research during the war of 1939-1945 caused a vast amount of chemical research to be centred upon the antimalarial drugs, and it is possible that, although antimalarial and antifibrillatory properties are not necessarily related, research carried out on the degradation products of antimalarials in the body in relation to metabolic and enzymal activities may yet shed light on the subject. Quinidine is described by DiPalma and Schultz in all its aspects. With regard to its toxicity, they warn that this depends largely upon the rate with which the drug enters the circulation. All service medical officers who have read instructions regarding the rate of injection of quinine into a vein should be well acquainted with this. Idiosyncrasy is another hazard to bear in mind. The possibility of embolism following the restoration of regular rhythm is also well known. Quinidine, as DiPalma and Schultz state, is a two-edged weapon, it may demand both boldness and caution, but today, when portable electrocardiographs have ceased to be unusual equipment, a careful and frequent check on the cardiac rhythm is a valuable and desirable safeguard.

One of the interesting possibilities of drugs appears in the recent use of quinacrine, better known as "Atebrin". Recent reports have been favourable of its power to arrest fibrillation; it may be given by the intramuscular route if necessary, but toxic reactions make its intravenous use risky. Though there is no constant pharmacological structure of the known antifibrillatory drugs, the common quinoline structure of some of the antimalarials may be a pointer to the discovery of better preparations. The South American drug α-fagarine, derived from a tree indigenous to Argentina, has been found to posses valuable cardio-depressant properties, and further study of its structure also may yield other drugs. Most of the other drugs which have been used for this purpose need no special mention here, beyond reference to the now well-known use of procaine as an antifibrillatory agent of definite value during anæsthesia or manipulations within the thorax. In conclusion, quinidine is still the drug of choice for the treatment of ectopic rhythms of the heart, in the opinion of DiPalma and Schultz, though they hope that medical chemistry will soon expand our resources.

[1] *The Journal of Bone and Joint Surgery*, February, 1950.

[1] *Medicine*, May, 1950.

Abstracts from Medical Literature.

OPHTHALMOLOGY.

Di-Isopropyl Fluorophosphate (DFP) and Glaucoma.

W. CONRAD STONE (*Archives of Ophthalmology*, January, 1950) reports on the use of di-isopropyl fluorophosphate on 150 glaucomatous eyes in 121 patients in a two-year period. A 0·2% solution in peanut oil was used. Of 78 eyes with signs and symptoms of chronic non-congestive glaucoma or acute exacerbations of this disease, 52 were benefited by the treatment. Of nine eyes with acute congestive glaucoma, three were benefited. Of 34 eyes with secondary glaucoma after cataract extraction, the condition in 25 was controlled. Of the total series of 150 eyes, 90 were benefited. Other treatments had previously failed. Pain and diminished vision due to ciliary spasm were experienced by 40% of patients, but in only 3% did therapy have to be discontinued. In 24 cases rise in tension occurred. The author states that the drug must be used with caution and the patient kept under observation even though the initial response is good.

Ocular Contusions in National Emergencies.

BRITTAIN F. PAYNE (*The Journal of the American Medical Association*, January, 1950) points out that in the event of a national emergency contusions of the eye will be one of the major causes of ocular disability. Contusions are non-perforating wounds caused by blows or explosions in which the fibrous tissue, the cornea and sclera, remains intact. The ocular changes that may occur are œdema and hæmorrhage in the eyelids, hæmorrhages in the conjunctiva, œdema and erosions of the cornea, wrinkling and rupture of Descemet's membrane, hyphæmia, iridodialysis, rupture of the iris sphincter, traumatic iridocyclitis, paralysis and spasm of accommodation, subluxation of the lens, cataract, hypotony and hypertony, vitreous hæmorrhage, rupture of the chorioid and chorioidal hæmorrhage, *commotio retinæ*, detachment of the retina and rupture of the *lamina cribrosa* and injury to the optic nerve. In the treatment of contusions many will heal completely after cleansing, bandaging and rest. It is dangerous to administer atropine. If the injury is severe the patient should be kept in hospital until the true nature of the injury is known.

Aureomycin in Ophthalmology.

JOHN G. BELLOWS *et alii* (*American Journal of Ophthalmology*, February, 1950) have treated 41 patients with aureomycin. For external ocular infections treatment was local with instillation of aureomycin borate 0·50% or aureomycin ethylene diamine 1·25%. The antibiotic was used at three-hourly intervals, except for three patients with severe acute epidemic kerato-conjunctivitis, in whom application was half-hourly for the first day of treatment. For blepharitis an aureomycin ointment was used. For intraocular inflammation aureomycin hydrochloride was given by mouth in divided doses totalling from 200 to 750 milligrammes per day. In staphylococcal conjunctivitis and blepharitis the response to treatment was good. A case of acute conjunctivitis due to a mixed infection of *Streptococcus viridans* and *Staphylococcus albus* did not respond. Similarly no response occurred in a case in which *Bacillus subtilis*, *Staphylococcus albus* and a diphtheroid were isolated. Rapid cure was effected in one case due to *Hæmophilus influenzæ*. Seven patients with epidemic kerato-conjunctivitis responded rapidly to treatment with aureomycin. The drug also proved of value in the treatment of trachoma; of two patients with episcleritis, one treated systemically recovered in two days and one treated by local instillation made no response. Two patients with acute iritis recovered after forty-eight hours of systemic therapy, but a patient with bilateral chronic uveitis failed to respond after one week's treatment. The authors regard aureomycin as the drug of choice in certain viral diseases of the eye, and state that it should be used in bacterial infections of the eye when sensitivity tests indicate the causative organisms to have a greater susceptibility to aureomycin than to other chemotherapeutic agents.

Occlusion of the Central Retinal Artery following Anæsthesia.

ISADORE GIVNER AND NORMAN JAFFE (*Archives of Ophthalmology*, February, 1950) report four cases of occlusion of the central retinal artery following anæsthesia. In analysing these cases they concede that a combination of three factors is needed, namely, loss of blood and shock, pressure on the eye in a patient with a low nasal bridge, and prolonged anæsthesia. They report these cases so that this complication may be prevented if the possibility is borne in mind.

Prevention of Retinal Venous Occlusion.

BERTHA KLIEN (*American Journal of Ophthalmology*, February, 1950) discusses ambulatory dicoumarol therapy in the prevention of venous occlusion. She states that the types of venous occlusion which promise most favourable results from this therapy are those which arise from a combination of two different pathological factors: a certain amount of narrowing of the venous lumen with an abnormal readiness for thrombus formation. Advancing obliterating sclerosis alone results in a kind of occlusion in which anticoagulant therapy is of little or no value after the completed event, as thrombus formation is only the terminal step, bringing about complete obliteration of an already slit-like venous aperture. Sufficient delay of this final event to permit establishment of an efficient collateral circulation, if this is possible, holds the only promise for preservation of vision, and can be attained in many cases by prompt and prolonged administration of dicoumarol after the first signs of venous circulatory impairment have become manifest. The danger signals of imminent retinal venous occlusion are intermittent visual obscuration or a slight constant reduction in visual acuity. The visual obscurations are due to œdema, which may not be visible ophthalmoscopically. The objective signs are engorgement of the venous circulation and œdema of the corresponding sectors of the optic papilla and possibly of the retina along the involved veins. Another finding of great diagnostic value is a dilatation or new formation of very tortuous vessels in one or more places at or near the optic disk. In preventive use of dicoumarol, the length of time over which it is used is of greater importance than a radical reduction of the prothrombin level to 20% or 25%, such as is necessary for curative purposes. The preventive management may be started with curative doses during the patient's initial period in hospital, combined if necessary with heparin, and continued on an ambulatory basis with a prothrombin level of 50% for many months or years. Preventive therapy has two main objectives—to gain time for the development of patent collateral channels and to permit repair of damaged venous endothelium by reducing strain upon the vessel wall. During ambulatory treatment biweekly or weekly prothrombin determinations should be carried out.

The Principles of Surgery on the Extraocular Muscles.

HERMANN BURIAN (*American Journal of Ophthalmology*, March, 1950) discusses the choice of operation in concomitant strabismus. He states that recessions are more effective than resections, and the immediate post-operative result in recession represents the end-result. He is against recessing both internal recti at the same sitting, as in his opinion the result is divergence. Resections are of no avail unless 10 to 12 millimetres of muscle are resected. The author considers it good treatment to respect both homonymous muscles at the one sitting, that is, both internal or both external muscles. Multiple operations are preferable to attempting too great a correction at the one operation. It is advisable to operate early if a functional cure is desired, although the author rarely operates before the patient is aged three years. For alternating convergent strabismus he recommends bilateral resection of the external rectus if there is no excess of adduction. For alternating divergent squint the operation of choice is a bilateral resection of the internal rectus muscle. In divergent squint an over-effect should be aimed at, this effect being achieved by resection.

Treatment of Retinitis Pigmentosa.

SAMUEL L. SALTZMAN AND CHARLES HAIG (*Archives of Ophthalmology*, March, 1950) carried out a special study to evaluate the treatment with cod liver oil and placental implantation of *retinitis pigmentosa*; Filatov had claimed successful results. They studied 47 patients with *retinitis pigmentosa* and two with *retinitis punctata albescens*. Of these patients 22 received cod liver oil injections only and 27 received cod liver oil and placental implantation. The results of treatment were checked by four criteria, namely, measurement of light sensitivity of the retina, visual acuity and visual fields, and the patient's comments on his ability to see. Of the patients receiving cod liver oil injections only, improvement in visual acuity was negligible. The visual fields showed little gain in most cases. In

the group who received cod liver oil injections and placental implants, increases in visual acuity were negligible. In some there was a decrease in visual acuity. The visual fields showed no significant change. The percentage of decreases in light sensitivity of the retina was greater than the percentage of increases. These results fail to support the results claimed by Filatov and his co-workers.

OTO-RHINO-LARYNGOLOGY.

Otological Findings in Acoustic Nerve Tumours.

P. E. IRELAND (*Annals of Otology, Rhinology and Laryngology*, September, 1949) presents a study of 92 patients who were operated upon in Toronto University Hospital and who were all proven by pathological examination to have acoustic neuroma. The survey was carried out in order to determine what useful information could be obtained from the otological findings. In this series deafness was the most outstanding single symptom, yet in 14 out of 92 proven cases there was no clinical history of this complaint. Tinnitus was complained of by only about half the patients with deafness. Vertigo was a rather late symptom, and in only two cases were there explosive attacks of the type usually associated with labyrinthine hydrops. In one of these complete loss of caloric response was found, with incomplete response in the other, while in both there was complete nerve deafness. The author feels that there should be no real confusion between Ménière's symptom complex and this lesion. Facial paralysis occurred in a moderate number of cases, but was usually of the mild type of paresis only. In the group of 77 patients who complained of deafness, the duration averaged 3·3 years. In 33 of these cases an adequate otological examination was recorded; in 25 complete nerve deafness was found, with complete loss of caloric responses in 20 and pronounced hypofunction in the remainder. Four patients had partial nerve deafness and complete loss of caloric response, and two had no nerve deafness, but had loss of caloric response. There were three patients without nerve deafness. Of 14 patients who did not complain of deafness, tests revealed four with partial nerve deafness and complete loss of caloric response and two with partial nerve deafness and normal caloric responses. In one case both hearing and caloric responses were normal, and in another there was only slight low-tone deafness with normal caloric reactions. Other neurological findings indicated a subtentorial lesion, probably in the cerebello-pontine angle, while X-ray examination often indicated an enlarged internal auditory meatus. While the examination of the auditory and vestibular portions of the eighth nerve may aid greatly in the localization of subtentorial tumours, the otological findings do not always follow the prescribed pattern in a certain number of proven tumours of the eighth nerve.

Osteoma of the Frontal Sinus.

A. J. VADALA AND K. SOMERS (*Archives of Otolaryngology*, November, 1949) state that while numerous cases of osteoma of the frontal sinus have been reported by a number of surgeons, the condition is nevertheless a comparative rarity, although probably many of the smaller osteomata are not reported and many are asymptomatic. The condition is most frequently encountered after the third decade and is much commoner in males. Almost every area in the frontal sinus has been reported as the site of attachment. In general the tumour is very slow in growing, although the rate may be faster in persons of the earlier age group. Some have been followed for years with little or no appreciable change in size. Osteomata at times tend to recur after removal. The incision for removal of the tumour should be such as to give adequate exposure and leave as little post-operative deformity as possible. It is generally agreed that where there is a likelihood of a dural tear, the approach is best made from the dural side. The tumour is usually attacked by chiselling it free, or partly free, and then rocking it loose with large rongeur forceps. If the sinus is not infected, one should not remove its lining or interfere with the fronto-nasal duct, although at times some steps may be called for to maintain the patency of the duct. Three cases are presented together with radiographic illustrations and a description of the steps followed in removal of the osteoma and subsequent drainage.

Surgery at the Base of the Tongue by Translaryngeal Approach.

GEORGES PORTMANN (*Archives of Otolaryngology*, October, 1949) states that the principal indication for surgery at the base of the tongue by translaryngeal approach is tumour of the epiglottic region and base of the tongue with or without involvement of the glosso-tonsillar grooves and inferior poles of the tonsils. A classic total laryngectomy may be necessary when the larynx is involved. After the larynx has been removed, the body of the hyoid bone is then removed. After this there is opened an extremely easy route to the hypopharynx, the base of the tongue and the tonsils. The base of the tongue may be grasped and pulled into the operative opening and appropriate resections may be made. The operation is finished with the formation of a pharyngostomy by suturing together the skin of the neck to the mucous membrane of the pyriform sinuses and laryngeal vestibule below and at the base of the tongue above. With less extensive laryngeal involvement the technique is modified by limiting the operation to the upper part of the larynx, even with maintenance in some instances of the integrity of the vocal cords and the arytænoids. A "T"-shaped incision is made, crossing just above the hyoid bone and passing downwards in the mid-line to the superior edge of the cricoid cartilage. The subhyoid muscles are cut close to the hyoid bone and from the laryngeal skeleton on its lateral aspect, close to the thyreoid cartilage. Through a transverse incision into the thyreoid cartilage, a few millimetres from its upper edge, the larynx is opened, and with scissors an oblique section of the thyreoid ala is removed. This makes an opening into the laryngeal vestibule above the vocal cords and exposes the posterior parts of the aryepiglottic folds. The anterior fragment of the laryngeal skeleton on which the epiglottis rests is held securely with a pair of Museux forceps. The pre-epiglottic layers are next resected between the epiglottis and hyoid bone. The hyoid bone may also be removed. Then the base of the tongue may be firmly secured with forceps and delivered through the operative opening by easy traction. The precise limits of involvement may readily be determined, and resection of diseased tissue with a normal surrounding margin is possible. Through the pharyngeal stoma which is made there is opportunity to observe healing and to place tubes of radium if this is thought necessary.

A Bronchial Fistula Terminating in a Tubulo-Dermoid Cyst.

N. W. GILL (*The Journal of Laryngology and Otology*, February, 1950) states that from a small sinus on the right side of the neck an intermittent purulent discharge was noticed, present as long as the patient, a man, aged thirty-one years, could remember. About six months before examination he had noticed a swelling on the right side of the throat, the external opening being about two inches above the sterno-clavicular joint. From this point a cord could be felt extending upwards to the region of the hyoid bone. A cystic swelling about the size of a large grape hung down from above and behind the tonsil of the same side. X-ray examination after lavage of the fistula for several days and then injection of lipiodol showed that the track of the fistula terminated in the cyst. Excision of the fistula was commenced from below after passage of a ureteric catheter for a distance of about two inches. A second horizontal incision was made in the skin fold one inch below the mandible. At this point the fistula appeared to have a complete muscular investment, and this with the contained track was separated downwards until junction was made with the portion already freed below. The dissection was then carried further upwards, the various anatomical structures being identified and separated until the fistula was found to take a sharp bend towards the pharyngeal wall, appearing to hook over the glosso-pharyngeal nerve and posterior to the stylo-pharyngeus muscle. The cyst was next dissected out from the tonsillar fossa, and the track was found to pass through the posterior faucial pillar and thence to the portion already dissected out in the neck. Healing was uneventful. The author states that bronchial fistulæ have been divided into four groups: (i) the complete fistula opening internally and externally; (ii) the incomplete fistula opening internally; (iii) the incomplete fistula opening externally; (iv) the cyst. The case reported belongs to group (ii). Bronchial fistulæ have been reported at all ages. They may show a strong familial tendency. The classical course taken is as described in the case reported, although the external opening may be higher in the neck and the interval below the tonsil. The fistula is lined by columnar and squamous epithelium. Occasionally Hassall's corpuscles have been reported in the walls, this finding being quoted in support of the theory that their origin is from the thymic duct. A bronchiogenic origin is otherwise supported from the anatomical dissections.

Special Article.

THE PREPARATION, DISTRIBUTION AND USE OF ANTI-RUBELLA GAMMA GLOBULIN.[1]

ANTI-RUBELLA γ GLOBULIN is prepared from the serum of persons convalescent from rubella (German measles), with the object of preventing, if possible, by its administration to the mother, the damage to the fœtus known to result from maternal infection with rubella during the early months of pregnancy.

As the Red Cross Blood Transfusion Service is a body suitably organized to recruit and take blood from volunteers willing to give their blood after an attack of rubella, for processing into γ globulin at the Commonwealth Serum Laboratories, the National Blood Transfusion Service Committee of the Australian Red Cross Society appointed two of its members (F. G. Morgan and L. M. Bryce) as a subcommittee, on which Professor F. M. Burnet, Director of the Walter and Eliza Hall Institute of Medical Research, and Dr. H. McLorinan, Medical Superintendent, Queen's Memorial Infectious Diseases Hospital, Fairfield, were invited to sit as coopted members, to consider and furnish a report on this subject to the committee.

The report and recommendations of the subcommittee were presented at a meeting of the Red Cross National Blood Transfusion Service Committee in February, 1950. At the request of this committee, and with the approval of the National Council of the Australian Red Cross Society, they are published (in slightly abridged form) as shown below for the information of medical practitioners.

1. It must be stressed at the outset that there is as yet no known laboratory means of determining the time of development of rubella antibodies in relation to the onset of the infection, the titre they are likely to reach and their persistence in the blood, or the period of retention of adequate potency of the prepared γ globulin. There has not been opportunity to make clinical trials under controlled conditions, which should provide sufficient data on which to base recommendations concerning the use of this material.

2. At the present time, therefore, such recommendations can only be made in the light of analogies suggested by the known facts concerning development of other viral antibodies (for example, influenza) and the results of the use of γ globulins or convalescent serum as protective agents against other viral infections (for example, in measles).

3. It is impossible to give a precise figure of the risk to the fœtus attaching to an attack of rubella at different stages of pregnancy, but it has been computed that the concentrated epidemic of 1940 in New South Wales caused abortion, stillbirth or clinically recognizable abnormality in about 25% of fœtuses of mothers infected during the first trimester.

4. Anti-rubella γ globulin first became available in Victoria about two years ago, following the collection of blood from convalescent rubella patients among the personnel of the Flinders Naval Depot in September, 1947. Since that time 300 women exposed during the first four months of pregnancy to direct contact with cases of rubella have been given intramuscular injections of two millilitres of this material within a few days of contact. On a reasonable estimate between 50 and 100 of these women would have been expected to contract the disease. It has, however, appeared in recognizable form (that is, with typical rash) in only five cases, occurring between December, 1948, and the present time. There was no factor common to these cases, such as a relatively long interval between contact and administration of the γ globulin, which was not also present in some of those who escaped infection, but all five had had intimate rather than slight contact with the infected persons—for example, with the husband as the source of infection in three cases. The procedure therefore appears to have prevented overt infection in at least 90% of potential cases. A follow-up of the infants has recently been initiated, but there is not yet sufficient information regarding any congenital defects on which to comment.

5. In view of these results, the subcommittee, while fully aware of the desirability of obtaining more exact information by controlled clinical trials, is of the opinion that in spite of the lack of precise data at the present time, women exposed to the risk of infection with rubella during the first four months of pregnancy should be given γ globulin obtained from the blood of persons recently convalescent from the disease.

6. It is recognized that there is often difficulty in making a certain diagnosis of rubella in isolated cases. The subcommittee considers therefore that the only satisfactory source of supply of convalescent serum is from groups of persons in which a definite diagnosis can be made on epidemiological grounds. Suggested sources of such groups are service camps, institutions with large staffs, possibly gaols *et cetera*, the first-named being particularly suitable.

7. The subcommittee therefore recommends that the Director of the Naval Medical Service, and the Directors-General of the Medical Services of the Army and Air Force, who have already officially sponsored the enrolment of service personnel as Red Cross blood donors for general purposes, should be asked by the Medical Director, Australian Red Cross Society, to extend their cooperation to embrace the "rubella project" by provision of facilities for and encouragement of enrolment of convalescents to give their blood in the event of outbreaks of rubella in service establishments in any part of Australia in which suitable arrangements can be made for its collection and transmission to the Commonwealth Serum Laboratories for processing. (In Victoria, with the approval and cooperation of the appropriate naval and military authorities, groups of volunteers from the Flinders Naval Depot and the Balcombe Army Apprentices' Camp have already visited the Red Cross Blood Transfusion Service to give their blood for this purpose.)

8. Epidemics of rubella among such groups would also probably provide the most suitable material for adequately controlled clinical trials, and it is recommended that the service medical directors also be asked to facilitate such trials when suitable opportunity arises. Any proposal to undertake such trials should be referred to this subcommittee for consideration.

9. The Commonwealth Serum Laboratories are able to process any reasonable amount of blood, that is, such as would be available on the lines indicated above, from any part of Australia. It is, therefore, recommended that, service or other necessary approval having been obtained, the divisional directors of the Red Cross Blood Transfusion Service should arrange for the collection of blood from groups of volunteers in their respective States, and its transmission to the Commonwealth Serum Laboratories for processing. The subcommittee considers (on theoretical grounds) that the optimum time to collect blood, with regard to high antibody titre, is about three to four weeks after the onset of the illness, but that any period up to six months is permissible. (It has, in practice, been found that the sixth week after onset is usually the most suitable to advise.)

10. As a general policy, it is recommended that prepared γ globulin be returned from the Commonwealth Serum Laboratories to each divisional director in amounts proportional to the amounts of "raw material" received from him, with the reservation that one-third (*pro rata*) of all supplies should be retained for use in the proposed clinical trials.

11. The subcommittee considers that authority for ultimate distribution of the prepared γ globulin for the treatment of ante-natal cases should be vested in the divisional directors of the blood transfusion service. They could either accept the responsibility themselves of deciding the validity of requests for it from medical practitioners, or could delegate such responsibility. In Victoria, Dr. H. McLorinan has consented to act as controller of the use of the product, and all requests are made or referred to him.

12. Pending more definite information from clinical and epidemiological trials, the subcommittee recommends that the procedure regarding administration of the γ globulin should be as follows:

(*a*) It should be given to any registered medical practitioner requesting it for the treatment of a woman exposed to the risk of infection with rubella at any time from a date of possible conception till the end of the fourth month of pregnancy.

(*b*) Dosage: Two millilitres given intramuscularly is the dose arbitrarily adopted in Melbourne and recommended at present. (Titrations of the γ globulin in respect of influenza antibodies have indicated that the processing produces an eight-fold concentration of those originally present in the serum.) The question of a larger dose was discussed, but it was agreed that at present it would be best to adhere to the present dosage so as to ensure a wider availability of

[1] From the Blood Transfusion Service, Australian Red Cross Society, National Headquarters, 122 Flinders Street, Melbourne, Australia.

the γ globulin than would be possible if the dose were increased.[1]

(c) Time of dosage. In the present state of our knowledge, it is considered that administration as soon as possible after contact should be recommended, with a view to prevention of multiplication of the virus at the site of implantation. Since, however, infection of the fœtus must be through the blood-stream, via the placenta, this cannot take place until the virus invades the maternal blood-stream a few days before the appearance of the rash. Unavoidable delay in administration for a few days after contact need not, therefore, necessarily be a cause for alarm, and reassurance of the patient on this point seems justifiable.

(d) If a woman is exposed to more than one case of rubella at intervals longer than two or three weeks, at any time during the first four months of pregnancy, she should be given a further dose of two millilitres at each contact.

(e) Medical practitioners who are given the γ globulin should be asked to supply the details necessary for record and follow-up purposes, on forms provided with the γ globulin.

Summary of Recommendations.

1. Only persons from groups in which the diagnosis of rubella is certain on epidemiological grounds should be used as a source of anti-rubella γ globulins.

2. As service establishments are likely to be most suitable of such groups, the cooperation of the medical directorates of the services should be sought, in respect of both supply of volunteers to give blood and facilities for controlled clinical trials of the processed material.

3. Divisional directors of the Red Cross Blood Transfusion Service should be responsible for the collection of blood from suitable groups in their respective States, for its dispatch to the Commonwealth Serum Laboratories for processing, and for arrangements for the subsequent use of the prepared product.

4. The processed γ globulin should, as a general policy, be distributed from the Commonwealth Serum Laboratories to each divisional director in amounts proportional to the material received from him, with the reservation that one-third of all processed material be set aside for use in controlled clinical trials.

5. Dosage and time of administration are suggested.

F. G. MORGAN.
F. M. BURNET.
H. McLORINAN.
L. M. BRYCE.

[1] Since this report was presented, the dose given in Victoria has been increased to four millilitres.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held at the Royal Prince Alfred Hospital on May 18, 1950. The meeting took the form of a series of clinical demonstrations by members of the honorary medical and surgical staffs of the hospital. Parts of this report were published in the issues of September 9 and September 16, 1950.

Gynæcological Specimens.

DR. C. L. CHAPMAN presented three pathological specimens obtained at gynæcological operations. The first had been removed from a patient, aged forty-two years, who had had menorrhagia for some months and had undergone operation in the country. Her doctor had found large *fibromyomata uteri* and had performed subtotal hysterectomy with conservation of both ovaries on October 18, 1949. She had continued to bleed for two months after operation, and on being examined on December 3, was found to have a cauliflower growth of the *cervix uteri*; the right ovary contained a secondary carcinomatous nodule. Radium was applied vaginally one week later. Dr. Chapman mentioned two points of interest. The first was that as cancer of the cervix and uterine fibroid tumours were both common diseases, it should never be assumed that fibroid tumours were the sole cause of bleeding; a careful watch should be made for carcinoma of the cervix, especially the more hidden endocervical forms. The second was the occurrence of the very rare metastasis in the right ovary from the carcinoma of the cervix.

Dr. Chapman said that the other two specimens illustrated the need to exclude carcinoma when surgical cure of prolapse was performed. One was from a woman, aged thirty-eight years, who had had procidentia with no apparent disease of the *cervix uteri*; however, microscopic examination of the cervix after removal in a Fothergill operation revealed an early carcinoma. Dr. Chapman pointed out that the removed cervix in Fothergill's operation should always be examined pathologically.

The other specimen was from a woman six months past the menopause who had presented herself for *procidentia uteri*. She had had one "spotting" of blood a week previously. At operation curettage produced very little material. Fothergill's operation was performed, but microscopic examination of the scrapings revealed carcinoma of the uterine body. Abdominal hysterectomy was performed two days after the result of the biopsy was known. A small carcinoma not as large as a threepenny piece was found in the left cornu of the uterus; it could have been revealed only by the use of Recamier's curette. Dr. Chapman said that the case taught the lesson that routine curettage with microscopic examination of scrapings was essential in all cases in which cure of prolapse was to be undertaken.

Simultaneous Ruptured Tubal Gestation and Twisted Parovarian Cyst.

DR. M. BRITNELL FRASER presented specimens and slides of simultaneous ruptured tubal gestation and twisted parovarian cyst. The patient, who had undergone operation on February 5, 1950, was a *primipara*, aged thirty years, with no pregnancy for seven years. Her symptoms were irregular vaginal bleeding for four weeks and severe lower abdominal pain two weeks previously. Four hours before admission to hospital she suffered very severe abdominal pain, accompanied by collapse. Before operation the diagnosis of leaking tubal gestation was made. At laparotomy, an interesting pelvic pathological state was discovered. The right Fallopian tube was the seat of a tubal pregnancy; it had ruptured, and the pelvis was filled with blood clots. The left ovary was infantile, measuring one by one-half centimetre, without evidence of follicle formation. The left tube was abnormally long, and its distal end stretched above the pelvic brim to a mass surrounded by adherent omentum. On separation of the adhesions, a twisted cystic tumour, measuring ten by four centimetres and situated in the outer part of the mesosalpinx, was revealed and dissected out. The abnormally long left tube was turned to the right and sutured to the back of the uterus by means of a fine stitch close to the right ovary.

Dr. Fraser made the following points: first, the rarity of the two acute pelvic conditions occurring simultaneously; second, the necessity for a thorough exploration of the pelvic cavity in all cases; third, the interesting anomaly of an infantile ovary and a parovarian dermoid on the same side (parovarian dermoids being extremely rare); and last, an attempt to overcome future sterility by suture of the long left tube close to the right ovary; that he thought of doubtful value, because a second tubal implantation might occur.

Endometriosis.

Dr. Fraser then demonstrated histological slides of endometriosis. The first, which showed an endometrial cyst one centimetre in diameter situated deep in the stroma of an enlarged cervix, was from a patient, aged forty-five years, who had had a total hysterectomy for severe menorrhagia. Dr. Fraser mentioned that occasionally such cervical endometriomata extended to the vaginal aspect of the cervix and might be mistaken for cervical carcinoma.

The second group of slides were from a patient whose condition was diagnosed clinically as endometriosis of the utero-sacral folds. She was a *primipara*, aged thirty-eight years, whose only pregnancy had been twenty years previously, and who had presented herself with symptoms of increasingly severe dysmenorrhœa, menorrhagia and sterility. Pelvic examination revealed an enlarged, tender, fixed uterus. Both utero-sacral folds were tender, and several small nodules were palpable in the right fold. At operation, many small tarry nodules were visible in both utero-sacral folds and scattered over the vesical peritoneum. Histologically, adenomyosis was proved in the outer half of the uterine wall and in both utero-sacral folds, which

were excised with the uterus. Dr. Fraser mentioned that although hysterectomy and bilateral salpingo-oophorectomy were sufficient to cure the condition, he preferred to excise the superficial nodules in the utero-sacral folds when possible, believing that residual neuralgia and sacral backache were common in this condition and that excision of the folds prevented them. He stressed the point that the proximity of the ureter to the folds necessitated care in the dissection. If the rectum was adherent to the back of the uterus, he still performed total hysterectomy, opening into the vagina anteriorly and leaving the rectum adherent to the posterior shell of the cervix. He did not favour subtotal hysterectomy, but admitted its safety in cases with widespread adhesions. This would be followed later by endocervical enucleation with the cutting diathermy loop from below. Dr. Fraser commented on the undoubted increase in the frequency of this condition and agreed with the American idea that late marriage and limitation of the size of the family were underlying causal factors.

Basal Temperature Charts in Sterility.

Dr. Fraser then demonstrated the basal temperature charts of patients in two cases of primary sterility. The first patient, a *nullipara*, aged twenty-four years, had been married four years. Except for some excess in weight no organic abnormality was present. Her basal temperature chart showed a characteristic rise above the normal on the fourteenth day of a twenty-eight day cycle. The second chart was that of a *nullipara*, aged twenty-six years, with grossly irregular menstrual cycles, periods of amenorrhœa occurring alternately with prolonged menses. Only on four days in five months had her temperature reached 98·6° F., and an endometrial biopsy on one of those occasions revealed early secretory signs. Other biopsies showed no evidence of ovulation. Dr. Fraser was of the opinion that the outlook for pregnancy in the latter type of patient was poor. Reduction of weight by diet and thyreoid medication were the only therapeutic measures he favoured for the fat, sterile patient.

Radical Vulvectomy.

DR. MALCOLM STENING showed patients to illustrate the result of the extended radical vulvectomy according to the technique of Stanley Way. He said that six patients had been treated by this surgical method; all had been of late post-menopausal age, ranging from sixty-five to eighty-one years, and all, except one, had had advanced carcinomata of the vulva, which had spread to involve the regional lymph nodes. Two such patients were shown: one fully healed (aged sixty-five years) and one healed to the fourth-week stage (aged seventy-seven years).

The principles of the operation were discussed, and they were shown to differ from the radical excision previously performed in that: (*a*) the excision of the vulval area was considerably more radical and wider and there was no suture (the groin wounds were sutured and one expected primary healing); (*b*) the extirpation of the regional lymph nodes was more complete and included the upper or deeper nodes (the deep femoral node of Cloquet, the external iliac and the deep inguinal nodes), as well as the lower or superficial nodes (the superficial inguinal, the superficial femoral and the presymphyseal nodes); (*c*) the tissue of the excision of the vulval area and the lymph node dissection was removed *en bloc* in one stage; (*d*) the inguinal ligaments on both sides were resected. In the series of cases discussed it had been necessary in one to resect the lower third of the urethra because of the proximity of an advanced clitoral growth, and in another to resect the anus, because of the advancement of a large growth involving the fourchette. Dr. Stening commented that the age of the patient did not appear to be a bar to the successful performance of the operation, as the very elderly patient withstood the operation well. The post-operative period had to be carefully supervised in regard to wound infection, electrolytic balance, protein replacement, hypostatic and circulatory derangement, and renal function. Early ambulation was an essential feature of the conduct in these cases. Primary healing within six weeks was not possible without skilful, energetic and vigilant nursing care. The ultimate, fully healed result of the operation was cosmetically satisfactory, not incapacitating and fully functional. It would seem that this very radical procedure was a singular advance in the treatment of carcinoma of the vulva.

Double Uterus, Fibromyomata and Pelvic Cyst.

DR. J. CAMERON LOXTON presented a married woman, aged forty-six years, who had been pregnant twice but had miscarried each time; she had first noticed pain in the right leg two months prior to her admission to hospital. The pain was aggravated by walking, and a fortnight later was associated with swelling of the lower extremity which increased to such an amount that she was obliged to remain in bed for two to three weeks. She had menstruated regularly for seven days in every twenty-eight until her last period on March 13, 1950. On her admission to hospital on May 29, 1950, the right lower extremity was found to be very œdematous with a palpable thrombus in the anterior branch of the long saphenous vein. A somewhat irregular tumour was palpable in the lower part of the abdomen, extending from the pelvis to an inch or more above the umbilicus. The vagina was divided into two more or less equal parts by a complete mid-line septum, with a cervix located in each vaginal vault. The cervices were continuous with a large, hard, somewhat nodular tumour, extending over towards the left iliac fossa. Bulging downwards into the right posterior quadrant and filling up most of the cavity of the pelvis could be felt the lower pole of a large tensely cystic tumour. X-ray visualization of the genital tracts by utero-salpingography was attempted on two occasions, but owing to distortion and elongation of the vagina by the cyst, proved unsatisfactory. At laparotomy, the hard nodular tumour palpable in the left side of the lower part of the abdomen was found to be a double uterus, of the *uterus septus* type, containing several fibroid tumours about two inches in diameter. The uterus and vagina were pushed forward and to the left by a large thin-walled cyst, which was embedded amongst the structures of the right pelvic wall and broad ligament. It was roughly oval in shape and extended from the fascia covering the upper surface of the *levator ani* to the region of the ascending colon. During its growth it had pushed the ureter and the obliterated umbilical artery with the peritoneum medially, and had insinuated itself between the iliac vessels (which were seen arching over its antero-lateral convexity) and the iliacus and psoas fascia posteriorly. The caecum was lying on the upper pole of the tumour, which reached upwards as far as the commencement of the ascending colon. Access to the tumour was obtained by dividing the right round ligament and the ovarian vessels and opening up the broad ligament. To facilitate matters the uterus was removed by total hysterectomy and the incision extended along the line of the ureter. This structure together with the obliterated umbilical artery and the peritoneum was dissected medially. By use of the finger and occasional sharp dissection a line of cleavage was found, and the tumour was separated from under the great vessels and from the other structures of the pelvic wall. Both ureters were found to be closely associated with the uterine arteries at the level of the internal os, and at that point were so bound up with the cervical fascia that they might have been divided accidentally, had they not been deliberately looked for and dissected out before the uterine arteries were tied. Dr. Loxton commented that the case illustrated the occurrence of unilateral œdema of the lower extremity in association with a simple cyst of the pelvic wall, the multiplicity of developmental defects, the usual direction of growth of these tumours in relation to the ureter, and the anatomical difficulties that might be encountered in their removal.

Deep X-Ray Therapy for Carcinoma of Mouth or Pharynx.

DR. HAROLD HAM and DR. F. DUVAL presented four patients with extensive carcinoma of the region of the mouth or pharynx, all of whom had shown a good response to deep X-ray therapy.

Dr. Ham first presented a female patient, aged sixty-six years, who had first come under his care on November 10, 1947. At that time she stated that she had had a sore throat for a period of three months, and her voice had had a nasal quality for two weeks. On examination of the patient a very large ulcerating and fungating carcinoma was found on the right side of the fauces, involving the whole of the right side of the soft palate and the right pharyngeal wall and tonsillar fossa, and with slight involvement of the floor of the mouth and base of the tongue. The growth occluded the post-nasal space on the right side. There were no palpable cervical glands. A small portion of the growth was removed for biopsy, and the pathologist (Dr. G. F. Davies) reported that the growth was an atypical squamous epithelioma. It was considered that the growth was too extensive for radium therapy. Deep X-ray therapy was therefore given, from November 17 to December 19. The physical factors were 375 kilovolts and a tumour dose of 5000*r* given in thirty-two days, the radiation being applied through two lateral fields and a submental field. At the time of the meeting there was no sign

of active disease, but there was a defect in the right side of the soft palate. The patient had been referred to the Dental Hospital for an upper denture to be prepared with an extension to cover the defect.

Dr. Ham also presented a male patient, aged fifty-five years, who had reported to him on December 5, 1949. On examination the patient was found to have a fixed ulcer, some three centimetres in diameter, on the medial aspect of the left lower alveolus in the molar region. X-ray examination of the mandible showed an area of bone destruction in this area, which appeared to be due to direct extension of the ulcerated lesion. A biopsy was taken from the edge of the ulcer, and the pathologist reported that the condition was a squamous epithelioma. The decision had to be made concerning treatment, between surgical removal of the ulcer and the left side of the mandible, and radiotherapy. The patient decided against surgical excision. Because of the bone involvement, the lesion did not appear very suitable for radium treatment by either mould or implantation. Deep X-ray therapy, given as an intensive course with small fields, was therefore decided on, and this was given from December 28, 1949, to January 27, 1950. The estimated tumour dose was 5400*r* given in thirty days; two lateral opposing fields and an anterior field were used. At the time of the meeting the ulceration was healed, but it was being watched each month. X-ray examination would be made shortly to determine the condition of the mandible.

Dr. Duval showed a patient with carcinoma of the nasopharynx who had been treated by deep X-ray therapy. The patient was a Chinese and no history could be obtained. He was first examined in January, 1946. On examination the right half of the soft palate was pushed forward by a tumour growing in the post-nasal space. On palpation, this was firm and rounded and reached to the mid-line. The upper limit could not be traced. No enlarged glands were palpable. A biopsy was taken, and the pathologist reported that the tumour was a squamous-cell carcinoma. A course of deep X-ray therapy was given from February 18 to March 11, 1946, and the estimated dose to the tumour was 5400*r*. After treatment, the post-nasal neoplasm disappeared, but in July a recurrence was evident on the right tonsil and soft palate, and the patient had signs of nerve involvement. The abducent and hyperglossal nerves on the right side were paralysed and the auditory tube was blocked. It was felt that the nerve involvement was extracranial, and that further treatment was justified in view of the previous satisfactory response. Two lateral fields were employed, including the base of the skull, post-nasal space and upper part of the pharynx, and a submental field to increase the tumour dose on the palate. Signs of nerve involvement disappeared rapidly, and the patient had remained free of recurrence since then. The soft palate was scarred, but otherwise there was no evidence of post-radiation damage.

Dr. Duval also presented a patient, aged sixty-two years, who had reported to him on October 26, 1949. The patient then had a swelling on the left side of his neck which had been apparent for some weeks. On examination there was a huge mass of glands in the left upper part of the neck measuring nine by eight centimetres. On the left side of the tongue a large cauliflower tumour was present and was found to be about four centimetres in diameter at the base of the tongue extending down as far as the finger could reach. No biopsy was taken, but it was evident that the tumour was a carcinoma of the tongue, with secondary glands in the neck. The chances of cure were considered small, but treatment was felt to be worth while and was given in November, a tumour dose of 5000*r* being given to the primary growth and glands. In January, 1950, the glands were no longer palpable and the primary growth had almost disappeared. At the time of the meeting the glands were still not palpable, but an ulceration could be felt with the finger at the base of the tongue; this was almost certainly a recurrence. Good palliation, however, had been effected, and the patient had been back at work for six months.

Ruptured Spleen.

DR. A. S. JOHNSON showed four patients who had had ruptured spleens. The first was a male patient, aged thirty-three years, who had been admitted to Royal Prince Alfred Hospital on February 22, 1947, after having been knocked down by a tram. He was pale and shocked, but conscious, and complained of generalized abdominal pain, worse on the left side. Examination of the patient revealed general abdominal tenderness and some guarding greatest in the left hypochondrium. The pulse rate was 88 per minute and the blood pressure 120 millimetres of mercury (systolic) and 80 millimetres (diastolic). A diagnosis of ruptured spleen was made, and after blood transfusion had been started, the abdomen was opened through a long left paramedian rectus-splitting incision; the peritoneal cavity was found to contain a large quantity of blood from a ruptured spleen, which was removed, and the abdomen was closed. "Open" ether anæsthesia was used. Blood transfusion was continued during operation, two litres being given in all. Post-operative treatment included continuous gastric suction, intravenous administration of glucose-saline solution and penicillin therapy. Subsequent investigations included a blood count on March 11, which showed 3,950,000 red cells per cubic millimetre, a hæmoglobin value of 83%, 8300 white cells per cubic millimetre and 580,000 platelets per cubic millimetre. X-ray examination of the chest on March 10 revealed fractures of the fifth, eighth and ninth ribs on the left side posteriorly, and a small amount of fluid at the base of the left lung. The patient made a good recovery and had since been well and able to carry out his ordinary work. The case was one of primary rupture of the spleen following trauma.

Dr. Johnson's second patient was a man, aged twenty-four years, who had been admitted to Royal Prince Alfred Hospital on January 24, 1950. He gave a history of having been struck over the left lower ribs by a piece of rock during blasting at his work on January 17. He had experienced some pain over the ribs and in the left hypochondrium and had been absent from work for six days; then he had recovered sufficiently and was able to resume. On the afternoon of the day of resumption of work he had experienced sudden severe pain in the left hypochondrium, epigastrium and left shoulder, and had vomited once. He also felt weak and somewhat breathless. Eight hours after the onset of the pain he was admitted to hospital. Examination showed that he was pale and in some distress. His pulse rate was 140 per minute, but his blood pressure was recorded as 140 millimetres of mercury (systolic) and 80 millimetres (diastolic). There was general abdominal tenderness and pronounced guarding in the left hypochondrium. A diagnosis of ruptured spleen was made. Blood transfusion was commenced in the operating theatre, and with the patient under general anæsthesia ("Pentothal", curare, ether and oxygen) the abdomen was opened through a left oblique subcostal incision. A large amount of blood was present in the peritoneal cavity from a ruptured spleen, which was removed, and the abdomen was closed. In all five pints of blood were given. Post-operative treatment included Wangensteen gastric suction, intravenous administration of glucose-saline solution and penicillin therapy, and the patient made a good recovery. He had since resumed work, but had been troubled at times with left shoulder pain. Dr. Johnson said that this patient represented a typical case of delayed rupture of the spleen following trauma. At the time of the original injury there must have been either a small tear, which sealed off, or a subcapsular rupture with hæmatoma, which broke through the capsule a week later.

Dr. Johnson's third patient was a man, aged thirty-six years, who had been admitted to Royal Prince Alfred Hospital on March 12, 1949. While travelling in the front seat of a motor-car on the previous afternoon the patient had been involved in a collision and thrown forwards, striking his head on the dashboard. He had no recollection of any injury to the trunk at that time or subsequently. He had been a little dazed after the accident, but had been able to go home and had not appeared seriously injured. He stated that prior to the accident he had not been feeling well and had some dyspepsia and had noticed a black motion on one occasion some days earlier. At about 4.30 a.m. on March 12 (fifteen hours before his admission to hospital) he experienced sudden severe abdominal pain, first in the left iliac fossa, becoming generalized and persistent, and then worse on the right side and in the right shoulder. He had not vomited. On examination the patient was found to be moderately obese and not appreciably pale. His temperature was 98·8° F., his pulse rate 84 per minute and his blood pressure 160 millimetres of mercury (systolic) and 100 millimetres (diastolic). His tongue was furred, and there was some general fullness of the abdomen with tenderness and much guarding in the epigastrium and right hypochondrium. In view of the main incidence of signs related to the right side and a previous history of dyspepsia and possible melæna, a provisional diagnosis of ruptured duodenal ulcer was made. The abdomen was opened, with the patient under "open" ether anæsthesia, through an upper right paramedian rectus-splitting incision. The peritoneal cavity was found to be full of blood, and a tear could be felt in the spleen when palpated. A long left oblique subcostal incision was then made and splenectomy performed. Blood transfusion

had been commenced as soon as blood was found in the peritoneal cavity, and in all three litres were given. Post-operatively intravenous administration of glucose-saline solution and penicillin therapy were used, and streptomycin and sulphonamides were given four days after operation, when the patient's temperature had risen to 102° F. Gastric suction was used for a limited period when vomiting occurred three days after operation. The patient made a good recovery and was able to carry out his ordinary work. Subsequent investigations showed that the spleen weighed 320 grammes and was rough and hæmorrhagic externally; microscopically there was an appearance resembling chronic congestion with probable malarial pigment present. A blood count on March 16 revealed a hæmoglobin value of 102%, 13,600 white cells per cubic millimetre, 81% being neutrophile cells, and 507,000 blood platelets per cubic millimetre. The patient had stated that he had been treated for malaria while in the army. Dr. Johnson commented that the case had been an interesting one, firstly because of the misleading abdominal signs, and secondly because of the question of the actual causation of rupture of the spleen. The history of attacks of malaria together with enlargement of the spleen and the histological picture confirmed the diagnosis of malarial spleen. Then there had been the trauma occurring the previous day, and although there was no history of direct injury, it was possible that some indirect injury might have led to damage of the already abnormal spleen with an early delayed rupture.

Dr. Johnson's fourth patient was a man, aged twenty-nine years, who had been admitted to Manly District Hospital on January 8, 1947. He had a history of previous attacks of malaria and for a week had been subject to attacks of fever; two days before his admission to hospital examination of a blood film had shown the malarial parasite. When admitted to hospital he was complaining of abdominal pain, which had commenced twelve hours earlier, chiefly in the epigastrium and left hypochondrium, and vomiting. He had been referred to hospital by his own doctor with a provisional diagnosis of ruptured gastric ulcer. After admission he had improved somewhat and was kept under observation. A blood count had then shown 4,000,000 red cells per cubic millimetre, a hæmoglobin volue of 75%, and 7600 white cells per cubic millimetre; examination of a blood film revealed evidence of malaria (*Plasmodium vivax*). On the following day, however, he became more collapsed, and the pain was more severe. Examination of the abdomen showed some distension, with guarding and tenderness greatest in the left hypochondrium; he also had pain in the left shoulder. His blood pressure had fallen to 70 millimetres of mercury (systolic) and 40 millimetres (diastolic), and blood transfusion was commenced. A diagnosis of ruptured spleen was then made. The abdomen was opened through a long left paramedian rectus-splitting incision, "open" ether being used as the anæsthetic agent. A considerable amount of free blood and clot was present in the peritoneal cavity. Splenectomy was performed and the abdomen closed. Four litres of blood and two litres of serum were given in all before, during and after operation. Post-operatively he was given further intravenous infusion of glucose-saline solution and penicillin, as well as "Atebrin" tablets and vitamin *K* therapy. A blood count on January 10 revealed 3,300,000 red cells per cubic millimetre, a hæmoglobin value of 65% and 18,000 leucocytes per cubic millimetre. A platelet count on January 16 revealed 350,000 per cubic millimetre; the coagulation time was four and a half minutes and the bleeding time three minutes. On January 22 a blood count revealed 4,600,000 red cells per cubic millimetre, a hæmoglobin value of 75%, 11,000 leucocytes per cubic millimetre, 68% being neutrophile cells, and 600,000 platelets per cubic millimetre; the coagulation time was four and a half minutes and the bleeding time two and a half minutes; the result of a fragility test was normal. The pathologist reported on the spleen as follows:

> Macroscopic: A moderately enlarged spleen which weighs 270 grams. The capsule is torn off a considerable area. There are some very deep notches in the spleen, also a few clefts which do not appear to have been caused in vivo since there is no hæmorrhage around them. On section Malpighian bodies are well defined.
>
> Microscopic: In sections of the spleen there is seen to be widespread dilatation of sinusoids, and some increase in fibrous tissue between these. There are very numerous minute globules of pigment, mainly intracellular. They are very small and roughly spherical in shape. I have found no definite malaria parasites in specially stained sections, but the appearances are consistent with the diagnosis of malaria.
>
> Spleen: Malaria.

Dr. Johnson said that in view of the fact that during a period when malarial parasites were present in the blood this patient had suffered a ruptured spleen in the complete absence of any history of trauma, the case had been regarded as one of spontaneous rupture of a malarial spleen. A matter of interest related to the fact that the patient had always been regarded as a "bleeder"; he had bled after an operation at Sydney Hospital for hernia thirteen years before and again after one for recurrent inguinal hernia at Gloucester House three years before. Fortunately no bleeding had occurred after the splenectomy. He had remained well since recovery from the operation.

Medical Societies.

THE AUSTRALIAN ASSOCIATION OF CLINICAL PATHOLOGISTS.

THE second annual general meeting of the Australian Association of Clinical Pathologists was held in Brisbane on May 27, 1950.

At the business session the following office-bearers and committee were elected for the ensuing period of office: *President*, Dr. Lucy M. Bryce, (Victoria); *Vice-President*, Dr. J. V. Duhig (Queensland); *Honorary Secretary*, Dr. J. D. Hicks (Victoria); *Honorary Treasurer*, Dr. Elsie Abrahams (Victoria); *Committee*, Dr. J. Inglis (Queensland), Dr. V. Rudd (New South Wales), Dr. E. North (Victoria), Professor J. Robertson (South Australia), Dr. S. Michaels (Western Australia), Dr. M. Shoobridge (Tasmania). In response to an invitation from the British Association of Clinical Pathologists, Dr. A. H. Tebbutt (New South Wales) was unanimously chosen as the nominee of the Australian Association of Clinical Pathologists for election as Corresponding Member of the British association. An invitation was also received from the International Society of Clinical Pathology for nomination of an Honorary President from Australia for the International Congress of Clinical Pathology to be held in London in July, 1951. Dr. E. Thomson (New South Wales) was unanimously selected as the nominee of the Australian association for this office.

At the scientific session the following papers were read: "Enzyme Studies of Cervical Secretions", Dr. Noel Gutteridge (Brisbane); "A Case of Medullary Histiocytic Reticulosis", Dr. V. McGovern and Dr. Edgar Thomson (Sydney); "The Determination of Oxygen Capacity by the Ferricyanide Method", Dr. F. Courtice (Sydney); "The Epidemiology of Infantile Gastro-Enteritis", Dr. E. Singer (Brisbane); "A Case of Tuberous Sclerosis", Dr. J. P. Little (Brisbane); "The Neurogenic Factor in Rheumatic Inflammation", Dr. Michael Kelly (Melbourne) (by invitation); "Lamellar Cerebellar Degeneration Associated with Retinitis Pigmentosa and Cataracts", Dr. Oliver Latham (Sydney).

Correspondence.

POLIOMYELITIS AND ITS RELATION TO RECENT TONSILLECTOMY.

SIR: In reference to articles on the incidence of poliomyelitis following tonsillectomy (THE MEDICAL JOURNAL OF AUSTRALIA, August 12, 1950, page 241 *et sequentes*) the discussions on ætiology omit an important factor. Surgical trauma is duly considered, but the fact is overlooked that, during tonsillectomy using the Davis gag and endopharyngeal ether anæsthetic, there is intense activity of muscles innervated from bulbar centres.

It is recognized that activity of muscles in the pre-paralytic phase is a factor in determining the incidence of paralysis in poliomyelitis. Therefore, if tonsillectomy, causing vigorous activity of bulbar innervated muscles, were performed in the unrecognized pre-paralytic phase of an attack of poliomyelitis, then a case which, without operative interference, may have been mild, would present as a severe bulbar poliomyelitis.

Perhaps this, then, is the explanation of the statement: "The type of poliomyelitis following tonsillectomy is usually bulbar."

Yours, etc.,

56 Cunninghame Street,
Sale,
Victoria.
September 4, 1950.

J. M. BELL, M.B., B.S.

STREPTOMYCIN AND PHARMACEUTICAL BENEFITS.

SIR: I read with interest the letter in THE MEDICAL JOURNAL OF AUSTRALIA of September 2 of this year written by Dr. Harvey, Dr. White and Dr. Bayliss concerning streptomycin and pharmaceutical benefits. I think they have uttered a very real and grave warning about the dangers of using streptomycin in pulmonary tuberculosis without integrating its therapy into an overall plan of attack against the disease in each patient.

It is fast becoming evident that "P.A.S." is a necessary adjunct to the administration of streptomycin in order to delay the emergence of predominantly streptomycin-resistant strains, yet this drug, "P.A.S.", has not been included on the free list of the *Pharmaceutical Benefits Act*! Also the prescribing of two-gramme single doses of streptomycin, which is favoured by many authorities in an intermittent régime, is also now a matter of some difficulty.

It is not only in tuberculosis, but also in other conditions, such as wound and gastro-intestinal infections and "pyrexias of unknown origin", that there is a danger of this emergence of drug resistance by the organisms when antibiotics are used in their treatment. And a fact which tends to be overlooked is that streptomycin, the most available of these, breeds resistant organisms at the most alarming rate.

I do not suggest that such drugs as aureomycin, "Chloromycetin" and streptomycin be withheld from use in certain urgent cases, but I do think that in the light of our still uncertain knowledge, some method of greater control should be instituted; otherwise we are only encouraging the formation of a race of highly fortified germs and a race of therapeutically, as well as diagnostically, destitute doctors.

Yours, etc.,

R. MUNRO FORD.

Adelaide,
September 4, 1950.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Lectures by Professor Gilbert I. Strachan.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that, in conjunction with the Royal College of Obstetricians and Gynæcologists, the following two post-graduate lectures will be given by Professor Gilbert I. Strachan, M.D., F.R.C.P., F.R.C.S., F.R.C.O.G., Professor of Obstetrics and Gynæcology in the Welsh National School of Medicine, Cardiff, Wales, who is visiting Sydney shortly as overseas examiner for the M.R.C.O.G. examination:

Monday, October 23, "Pre-Cancerous Conditions of the Cervix", in the Stawell Hall, 145 Macquarie Street, Sydney, at 8.15 p.m.

Tuesday, October 24, "Displacements of the Uterus", in the lecture hall, the Women's Hospital, Crown Street, Sydney.

All medical practitioners are invited to attend these lectures.

Lecture-Demonstration at Balmoral Naval Hospital.

The Post-Graduate Committee in Medicine in the University of Sydney announces that Dr. R. J. Walsh will conduct a lecture-demonstration on "Recent Advances in Hæmatology" on Tuesday, September 26, 1950, at the Balmoral Naval Hospital, Balmoral, beginning at 1.30 p.m. Films and slides will be shown. Following afternoon tea, there will be a demonstration of interesting clinical cases by the staff of the hospital.

All members of the medical profession are invited to attend.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED SEPTEMBER 2, 1950.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.	Australia.
Ankylostomiasis	*	..	1	..	..	..	..	..	1
Anthrax	*	..	..	..	..	..	..	..	..
Beriberi	*	*	*	*	*	*	..	*	..
Bilharziasis	*	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	3(1)	..	..	..	..	1(1)	..	..	4
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(*a*)	*	*	..	*	*	*	*	*	..
Dengue	*	*	*	*	*	*	..	*	..
Diarrhœa (Infantile)	..	..	..	..	..	..	..	..	..
Diphtheria	7(5)	3(1)	1	..	7(6)	..	..	..	18
Dysentery (Amœbic)	*	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	*	1(1)	..	..	..	..	..	..	1
Encephalitis Lethargica	..	..	..	..	..	..	..	..	..
Erysipelas	*	*	*	..	*	*	..	..	..
Filariasis	*	..	..	..	..	..	..	..	..
Helminthiasis	*	..	*	*	*	*	*	*	..
Hydatid	*	..	*	*	..	*	*	..	..
Influenza	*	*	*	..	*	*	..	*	..
Lead Poisoning	*	*	1(1)	*	*	*	*	*	1
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(*b*)	*	..	1(1)	..	..	..	..	..	1
Measles	*	*	*	238(198)	*	*	..	1	239
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	16(14)	4	1	13(12)	..	..	..	..	34
Psittacosis	*	..	*	..	..	*	*	*	..
Puerperal Fever	..	..	1	..	..	..	..	..	1
Rubella(*c*)	*	*	..	*	5(4)	2(2)	..	..	7
Scarlet Fever	21(9)	14(10)	3	7(4)	3(3)	1	..	..	49
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	*	..	2	*	*	*	*	*	2
Trachoma	*	..	*	*	*	*	*	*	..
Tuberculosis(*d*)	20(14)	22(19)	9(5)	11(9)	11(6)	6(3)	..	..	79
Typhoid Fever(*e*)	..	..	..	..	..	..	..	..	..
Typhus (Endemic)(*f*)	..	..	1	..	..	..	..	..	1
Undulant Fever	..	..	..	..	..	..	..	..	..
Weil's Disease(*g*)	*	*	4	*	*	*	*	*	4
Whooping Cough	*	*	*	1(1)	*	*	..	..	1
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 37, 1946–1947. Figures in parentheses are those for the metropolitan area.
[2] Figures not available.
[3] Figures incomplete owing to absence of returns from the Northern Territory.
* Not notifiable.
(*a*) Includes Mossman and Sarina fevers. (*b*) Mainly relapses among servicemen infected overseas. (*c*) Notifiable disease in Queensland in females aged over fourteen years. (*d*) Includes all forms. (*e*) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (*f*) Includes scrub, murine and tick typhus. (*g*) Includes leptospiroses, Weil' and para-Weil's disease.

It is proposed to conduct similar lecture-demonstrations at monthly intervals throughout the year at the Balmoral Naval Hospital; details of these will be announced from time to time.

University Intelligence.

THE UNIVERSITY OF MELBOURNE.

THE following information is taken from the *University Gazette* of the University of Melbourne of September 4, 1950.

Dr. E. S. J. King, pathologist at the Royal Melbourne Hospital, has been appointed to the Chair in Pathology.

Dr. D. F. Gray has been appointed to the status of Associate Professor in the Department of Bacteriology.

Dr. G. C. de Gruchy has been appointed research scholar in hæmatology at Saint Vincent's Hospital, Melbourne.

Naval, Military and Air Force.

APPOINTMENTS.

THE following appointments, promotions *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 53, of September 7, 1950.

AUSTRALIAN MILITARY FORCES.

Royal Australian Army Medical Corps (Medical).

NZ208064 Captain (Temporary Major) D. C. Cook is seconded to the Department of Supply (Army Component), 4th August, 1949.

Citizen Military Forces.

Northern Command: First Military District.

Royal Australian Army Medical Corps (Medical).—The following officers are appointed from the Reserve of Officers, and to be Captains (provisionally), 6th July, 1950: Honorary Captains 1/39084 M. E. Lake, 1/39083 R. Cantamessa, 1/39085 G. C. T. Kenny and 1/39086 W. H. Tait.

Obituary.

STANLEY COCHRANE.

WE regret to announce the death of Dr. Stanley Cochrane, which occurred on May 25, 1950, at Mitcham, Victoria.

Nominations and Elections.

THE undermentioned have applied for election as members of the South Australian Branch of the British Medical Association:

Murphy, Thomas Roy, L.R.C.P. and S. (Edinburgh), 1932, 95 Watson Avenue, Toorak Gardens.

Linn, John Graham, M.B., B.S., 1950 (Univ. Adelaide), Royal Adelaide Hospital, North Terrace, Adelaide.

Harbison, John Henry, M.B., B.S., 1949 (Univ. Adelaide), Royal Adelaide Hospital, North Terrace, Adelaide.

Topliss, John George, M.B., B.S., 1950 (Univ. Adelaide), 18 Ranelagh Street, Woodville.

The undermentioned have been elected members of the South Australian Branch of the British Medical Association:

Milazzo, Stephen Charles, M.B., B.S., 1949 (Univ. Adelaide), Royal Adelaide Hospital, North Terrace, Adelaide.

McLeay, Ronald Barton, M.B., B.S., 1948 (Univ. Adelaide), 2 Oaklands Avenue, Royston Park.

The undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Torpy, Denys Clifton, M.B., B.S., 1948 (Univ. Sydney), Department of Biochemistry, University of Sydney, Sydney.

Medical Appointments.

Dr. J. G. Hurley has been appointed a member of the Hospitals and Charities Commission, in pursuance of the provisions of the *Hospitals and Charities Act*, 1948, of Victoria.

Diary for the Month.

SEPT. 26.—New South Wales Branch, B.M.A.: Ethics Committee.
SEPT. 27.—Victorian Branch, B.M.A.: Council Meeting.
SEPT. 28.—New South Wales Branch, B.M.A.: Branch Meeting.
SEPT. 28.—South Australian Branch, B.M.A.: Branch Meeting.
SEPT. 29.—New South Wales Branch, B.M.A.: Annual Meeting of Delegates.
OCT. 3.—New South Wales Branch, B.M.A.: Council Quarterly.
OCT. 4.—Victorian Branch, B.M.A.: Branch Meeting.
OCT. 4.—Western Australian Branch, B.M.A.: Council Meeting.
OCT. 5.—South Australian Branch, B.M.A.: Council Meeting.
OCT. 6.—Queensland Branch, B.M.A.: Branch Meeting.
OCT. 10.—New South Wales Branch, B.M.A.: Executive and Finance Committee; Organization and Science Committee.
OCT. 13.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney)—All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

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